

Panel Discussion on Microbiome

Researchers and industry experts are turning their attention towards the emerging relationship between the skin microbiome and healthy skin. This has the potential to revolutionise the beauty and personal care industry. Let's see how. In the next few pages Keyplayers in the field have been invited to comment on specific issues.

How can the germs on facial skin be analysed quantitatively and qualitatively, and compared from one person to the next? Are beauty-related (and NOT disease related, such as psoriasis, AD, dermatitis etc.) categories or microorganisms characterized? What does it all mean? And how can cosmetic products and/or ingredients help? Are there any studies yet available that show the beauty benefits of products that claim to address these questions? When is the "equilibrium" of the skin's microbiome considered to be disturbed, and how (with which products) can it be restored? And do the consumers really understand these concepts, do they in large numbers adhere to such claims and buy products based on them?

PANELISTS



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RECENT ADVANCES AND NEW STRATEGIES FOR SUBSTANTIATING MICROBIOTA-RELATED COSMETIC CLAIMS

Sabrina Leoty-Okombi, BASF Beauty Care Solutions

The skin is an ecosystem that is made up of different habitats rich in microorganisms, which are also known as microbiota. Of these microorganisms, commensal flora positively contributes to skin defence by producing defence molecules such as antimicrobial peptides (AMPs) and free fatty acids.

If the microbiota ecosystem is impaired, this can lead to changes in the skin. Several recent studies illustrate the relationship between the skin microbiome and the beauty and health of the skin. These studies demonstrate a change in the composition and repartition of microbial species that is correlated with aging and different skin conditions (e.g. acne and atopic-prone skin, dandruff). Several tools are now available to profile the skin microbiome.

Thanks to the genomic revolution, we can directly and specifically quantify the different microbial species by qRT-PCR. We can also study the global microbiome after swabbing or punching the skin thanks to metagenomic techniques. Moreover, microbial metabolites produced by different bacterial species can also be assessed using metabolomic analysis (LC-MS, GC-MS). However, biostatistical data analysis is required to provide evidence of the correlation between the skin microbiome and different skin conditions over time on each individual or between characteristic panellist's groups.

A positive correlation between *Staphylococcus aureus* and dry skin conditions out of the pathological conditions was proved in several studies. Aging is also another factor that can influence the skin microbiota composition. For example: data suggest that the age-related changes in the skin microbiome are dependent on the skin area and that the quantity of *Propionibacterium acnes* decreases over time while *Corynebacterium* increases (1).

Taking into account the origin of skin disorders and microbiota dysbiosis, we can envisage new active ingredients that would be able to rebalance the skin microflora or take advantage of the microbiome to contribute towards maintaining or recovering skin beauty.

One way to influence the skin microbiome is to use probiotics. Probiotic supplementation using commensal bacteria (*S. epidermidis*) has been shown to improve dry skin conditions. Furthermore, it has been observed that *S. Epidermidis* could also produce short-chain fatty acids to limit the growth of *P. acnes*, resulting in an improvement in skin quality (2). They are also able to modulate the maturation of adipocytes (3).

Furthermore, thanks to the benefits already demonstrated at the gut level of a maintained probiotic "equilibrium", consumer awareness and expectations have dramatically increased skincare products addressing the microbiote. Nowadays, the cosmetic industry doesn't have any choice other than to integrate new data and knowledge on the skin microbiota ecosystem into product developments.

That's why, to further explore the role of microbiota in the skin, we established an interdisciplinary Innovation Platform on skin microbiota. Using this new platform, we aim to better understand the role of each micro-organism in the context of skin beauty. We have developed clinical protocols and *in vitro* models to study the complexity of the skin's microflora and the skin's ecosystem to help design more specific solutions tailored to each and every skin condition.

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SKIN MICROBIOTA: MAINTAIN THE DIALOGUE

Mathieu Bey, BIOVITIS-Greentech Group

The skin microbiota is a unique ecosystem to each individual whose role in metabolic, immune and neurological functions is now established. Microbiota is specific and little differences can have an important impact on this ecological system and finally on the host. Recently, the term "holobiont" was used to define the man and his microbiota (1). Even if it doesn't exist a standard composition for skin microbiota, we can identify common genera (*Staphylococcus*, *Propionibacterium* and *Corynebacterium*) with variations on ratios, species and strain-level specificities (2).

Unbalanced skin microbiota clearly play a role in the pathobiology of many types of skin disease and cosmetic disorders. In fact, when the diversity is lost, some microbial populations take the lead instead of others and participate actively to increase disorders such as inflammatory process. In the case of psoriasis, the use of metagenomics method

showed decrease diversity and increase in *Staphylococcus* with potential strain-level variations as key determinants of the psoriatic microbiome (3).

To control and define the diversity, specific index are frequently used (i.e. Shannon index) to evaluate the diversity from individuals to another or during the evaluation of a product. The role of skincare is to maintain the homeostasis of the skin and its microbiota. The cosmetic industry has to take into account not exclusively the skin health of consumer and the naturalness of products use but also the compatibility with this micro-ecosystem to prevent any disorders.

For cosmetics, the beauty claim can also be the expression of the healthy status of skin. Such claims can be attributed to balance of skin microbiota, induction of commensal diversity to promote education of our immune system and protection against the environmental aggressions (an active ingredient from Greentech based on *Lactobacillus* extract promoting the balance of skin microbiota). If we want to grow efficiently our skin microbiota, we have to address the right compounds to create

the best microenvironment on skin. Clinical studies have to be done with evaluation of the status of skin microbiota before and after the application of active ingredient. Currently, there is no standardised methodology to control effects on skin microbiota and this aspect will be an important future challenge.

Three years ago, nobody, except scientific community, was writing on this topic. Today, with frequent press release, consumers are more and more aware about microbiota "in general". Cosmetic companies and press have a crucial role to explain what it cannot be seen at the surface of our skin.

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THE SKIN AND ITS MICROBIOME ARE ONE ENTITY

Harald van der Hoeven, CLR

The interest of the consumer seems to be switching to a 'health-approach', when it comes to their skincare regimens. The increasing popularity of so-called dermocosmetics illustrates this. Wellness is another topic enjoying increasing popularity. A 'healthy' skin microbiome clearly fits into these 'health-approaches'. The question therefore is, what is a healthy skin microbiome? And how can we make improvements in the skin microbiome? Is there room for improvement at all? What cosmetically relevant outcomes can be expected?

CLR Berlin's conviction is that, during the epidermal differentiation process, 'ingredients' (antimicrobial peptides, molecules which regulate skin surface pH etc.) are produced with which the skin manages its microbiome. Where this does not function well, the microbiome changes and becomes 'unhealthy' or at least 'different'. Inversely, the skin microbiome has an important influence on the skin and its functionality too. In a healthy situation, our skin exists in a homeostasis with its microbiome. Both influence each other positively, a positive feedback loop. In a less positive situation, this feedback loop can become a vicious circle, where one can negatively influence the other.

Probiotic bacteria are not able to live on skin, they live in the gut. They perform an identical role for our body, though. In the gut they live on the epithelial cells, which form a physical

and immunological barrier. The epidermis is a stratifying epithelium. Here we need a stratum corneum, but apart from that the keratinocytes in the epidermis perform an identical job to the epithelial cells in the gut, they form a physical and immunological barrier for our body.

Analogous to the skin and its microbiome, the probiotic bacteria in the gut and the epithelial cells they reside on, interact with each other. The nature of this interaction, in the gut and in and on the skin is, for an important part, the same; bacterial molecules interact with the human cells through receptors on the outer membrane of these cells. The epithelial cells and the keratinocytes show many identical receptors in this context. This relatively new realization helps to rationalize the notion that topical application of lysates of probiotic bacteria has shown to positively influence the functionality, 'health' of the skin. Just like the way the 'healthy' skin microbiome positively influences the skin. Lysates of probiotic bacteria (e.g. *Lactococcus Ferment Lysate*, *Bifida Ferment Lysate*) can be interpreted as mimicking a 'healthy skin microbiome'. They can improve skin overall.

As the consumer's interest in skin health is of growing importance, overall cutaneous health should be observed, not the skin microbiome and the skin as different entities. The human race might now well be called 'homo microbiens'. For each human cell our body is host to 1 to 10 microbial cells. For an important part we live in symbiosis with each other. We need each other. Healthy skin means healthy skin microbiome and vice versa. With many cosmetically relevant results.

THE SKIN MICROBIOME AND BEAUTY: CHANGING THE NARRATIVE ABOUT BACTERIA

Mathias Gempeler, DSM Personal Care

The skin microbiome as a beauty concept is certainly creating a buzz, but the topic is still very much uncharted territory for the personal care industry and consumers alike. At DSM we are determined to bring some clarity. To do this, we

have carried out an in-depth market and consumer study, embarked on original new scientific research and have also investigated the impact our established actives have on microbial related activity on the skin.

We have found that brands currently offering microbiome-related products are mainly focused on prebiotics and probiotics (extracts made from bacteria), with cosmetics

positioned as microbiome-friendly or microbiome-enhancing. From the consumer perspective, the idea of treating the skin as a living ecosystem sits well with wider trends for natural and holistic beauty, but the idea of bacteria as “bad” is still quite common. As product launches begin to arouse curiosity, this view is beginning to change but what our research has highlighted is a need for clear explanations about which products work, how they work and the beauty benefits they bring.

New scientific research will help to answer some of these questions in the future. Until recently, studies have focused on identifying microbes on the skin. But at DSM we want to understand more about the conditions in which microbes are either beneficial or harmful to the skin, what triggers imbalances in the skin flora and how can we rebalance these. Our research will combine our current and already well-established research on epidermal care, known as CORNEOCAR with a new approach to the skin microbiome. A strong epidermal barrier and balanced skin microbiome are both needed to restore, strengthen, and preserve beautiful skin. This is because the epidermis both provides the environment in which microbes thrive and acts as a barrier, protecting the body against bacterial infiltration. By focusing on the interaction of microbiota on facial skin and the scalp, and supporting biological processes in the epidermis, we can build a balanced and strong epidermal barrier to achieve a fresh, vibrant complexion or a hydrated, comfortable scalp.

We have already made encouraging discoveries about two of our well-established actives. Thanks to its mode

of action, the peptide derivative Benzylsulfanyl D-Seryl Homophenylalanine Amidinobenzamide Acetate can boost skin barrier strength by breaking the plasmin cycle in two ways. At microbe level, it has been shown *in-vitro* to act directly on *S. aureus*, reducing levels of the bacteria, and at molecule level, it has been shown to reversibly inhibit the serine proteases urokinase and plasmin. *In-vivo* studies back up the benefits of this action: after 29 days of using the peptide, volunteers showed a significant improvement in skin resilience, smoothness and hydration and reported reduced skin sensitivity.

The skin microbiome also has an impact on scalp condition because microbial infiltration can lead to inflammation in the epidermis at the hair shaft, weakening the skin barrier and exacerbating flaking skin here. The carbohydrate complex Saccharide Isomerate has been shown to balance microbial activity in the scalp barrier by influencing the equilibrium of species such as *Malassezia furfur* and *Staphylococcus epidermidis* in the scalp microbiome. The benefits of this are reduced dryness and irritation. Consumer test panels confirm that Saccharide Isomerate reduces flakiness and itchiness caused by dehydration, leaving the scalp softer, smoother, hydrated and more resilient ().

Our investigations into the skin microbiome have only just begun, but with such promising results already, we hope that this paves the way for further innovation.

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EVER WONDER HOW THE URBAN LIFE AFFECTS OUR SKIN MICROBIOTA?

Marie Ollagnier, Lubrizol Advanced Materials

A balanced cutaneous microbiota can provide vital functions, such as barrier protection, for a healthier and more protected skin. Through the direct competition for space and nutrients, the beneficial bacteria can cause the exclusion of potentially harmful bacteria. Also, the reciprocal interaction of the microbiota with keratinocytes helps enhance the innate immune response, allowing the recognition of pathogens to prevent their invasion. Disruption of this ecological balance, also termed dysbiosis, can result from several factors and lead to different skin disorders. The massive growth of urbanization became a turning point in the relationship of humans with their environment, reducing human interaction with nature. This important moment also represented a relevant trigger in the prevalence of inflammatory disorders, such as allergies and eczemas, making the individuals living in urban environments more prone to suffer from skin sensitivity. Research has shown that the current exponential growth of urbanization and the exposure to modern lifestyles may induce alterations in the cutaneous microbiota, such as a reduction in microbial diversity, that could make the skin more prone to sensitivity and discomfort.

The cosmetic industry is joining the currently growing trend of microbiota-inspired skin care by delivering innovative

products that aim to preserve the important bacteria-host homeostasis for a healthy and good-looking skin. A recently developed Lipotec™ Active Ingredients heptapeptide is intended to strengthen urban exposed and sensitive skin by favoring microbiota balance and diversity, and by improving the skin immune response and the physical barrier integrity. A metagenomics analysis on urban exposed volunteers showed that the ingredient helped increase the microbial diversity, it favored the balance of the microbiota and it modulated bacterial functional pathways with potential benefits for the skin, which are all markers of the healthy and protected skin of populations in closer contact with nature. Other clinical studies on urban volunteers showed the ability to reinforce cell cohesion and to reduce transepidermal water loss levels after damage, suggesting a protective effect of the skin barrier.

In vitro, the peptide showed to favor the adhesion of beneficial bacteria over that of pathogenic bacteria on keratinocytes and helped induce genes associated with the activation of the immune response to keep the skin ready in case of any potential invasion. An enhancement in tight junction genes and long-chain ceramides were also obtained, contributing to a well-preserved skin barrier.

The peptide helps strengthen the physical and microbial barrier function for a reinforced urban skin resembling that of our ancestors in closer contact with nature.

WHY PREBIOTICS ARE KEY FOR BALANCED SKIN

Rebecca Harris, Oat Cosmetics

The skin is naturally enveloped in its own microbiome and these are unique to each individual, with no two persons microbiome being completely identical. Each skin's microbiome plays a key role in the maturation and homeostatic regulation of keratinocytes and immune system with dysfunction of both from the environment and lifestyle choices, implicated in ageing processes and disease.

As our primary connection with the external environment, the skin's microbiome biodiversity is heavily influenced by many external factors, including the biodiversity of our intimate external and internal environments, lifestyle habits and exposures. These include poor diet, disease, excessive hygiene, smoking, cosmetics, pollution, UV exposure and drugs. It is the consequences of microbiome disturbances and composition that will also lead to increased skin (oxidative) stress, thus an increase in certain defined ageing parameters.

A well protected skin in terms of efficient barrier possesses a well-balanced microbiome. As previously mentioned, genetics, lifestyle choices, and the environment stress this balance, and so it is important to give the skin's microbiome additional support by ensuring that products applied to the skin promote this healthy balance, rather than detract from it.

One approach is to provide favourable conditions for the microbiome. Pre- and probiotic beneficial effects can be delivered topically or by ingestion. They have the capacity to optimise, maintain and restore the skin's microbiome. Probiotics with resident microflora can also produce antimicrobial peptides benefiting cutaneous immune responses. In cosmetic formulations, prebiotics applied to the skin should in theory, be able increase selectively the activity and growth of beneficial 'normal' skin microflora.

Whilst skin types, gender, age, and genetics mean it is impossible to create one solution to fit all microbiomes; providing the skin with a formulation containing a prebiotic mix of principle actives to enhance normalisation of the skins microflora, is an intelligent approach to addressing a number of skin conditions such as atopy and acne.

Oat Cosmetics has produced a new fermented prebiotic derived from its high performance patented colloidal oatmeal, utilising *Lactobacilli* cultures. This ingredient is a natural active containing a prebiotic complex of fermented oat derivatives which improve skin health and boost cell turnover. Topical use has a direct effect at the site of application by enhancing the skin's natural defence barrier, speeding up the recovery of the skin's first line of defence and enhancing the conditions for the microbiome to thrive. This ingredient offers further skin benefits including an improvement in skin complexion and radiance whilst also plumping and firming the skin.

THE DAWN OF A NEW AWARENESS....

Dario Zanichelli, Phenbiox srl

The new tools of Next Generation Sequencing are opening up a new and complicated world to the eyes of cosmetic science. The skin is no longer just the organ that separates us from the outside world, but the habitat of an incredibly varied ecosystem greatly influenced by the environment that surrounds us and on which our well-being depends (1). The literature on this topic is still very limited and somewhat confused, but it is becoming increasingly clear that the unbalances in microbiota are closely correlated with a number of local and systemic disorders (2).

To fully understand the importance of this new science, considering also that each of us has our own unique microbiota, we need much more time, research and, presumably, given the huge amount of data to be handled and analysed for every single microbiota test (never mind for microbioma, even more complicated!) the adoption of relatively new tools such as Big Data analysis.

What seems to be well-established, however, is that a high biodiversity of microbiota is a positive element while, on the contrary, skin problems, such as dermatitis

or psoriasis, for example, present a less varied microbiota. Another aspect that seems to be gaining ground is that the greater abundance of certain families/genera of microbiota is associated with a healthier skin condition (3).

The causal link between skin conditions and microbiota conditions is not yet clear, and in view of the fact that it no longer seems possible to consider these two elements separately, perhaps it no longer makes sense to wonder whether the chicken or the egg came first. It does, however, seem certain that the potential effects of cosmetic ingredients on microbiota must be taken into serious consideration.

At Phenbiox, we decided to start exploring this fascinating new world, evaluating the effects that some of our ingredients can have on the skin, even in terms of an impact on microbiota:

One of our ingredient based on *Vitis vinifera* fruit extract, *Zingiber officinale* root extract, *Boswellia serrata* resin extract is a purifying, soothing, and conditioning natural and preservative free active ingredient able to help the skin and the scalp to re-balance dysbiosis of skin microbiota, without altering the physiological condition of the skin, reducing imperfections, redness and unpleasant sensations related to acne and dandruff. On healthy

skin, this product confirmed its mildness not depleting the biodiversity of the microbiota.

Another ingredient based on microencapsulated grapevine sap (INCI: *Vitis vinifera* vine sap), is an extremely well-balanced mix of nutritional substances able to effectively feed the plant, the skin and also the microbiota. This active ingredient not only nourishes and stimulates the skin, improving elasticity and moisturisation, but it is also able to positively modulate the skin microbiota composition without reducing its biodiversity.

A new awareness regarding the importance of the travelling companions that populate our skin is rapidly becoming established and I do not think this will prove to be just a passing fad in the cosmetics world.

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IS THE USE OF CURRENTLY AVAILABLE TOOLS FOR MICROBIOME SEQUENCING SUFFICIENT TO UNDERSTAND THE FACIAL MICROBIOTA?

Stefan Hettwer, RAHN AG

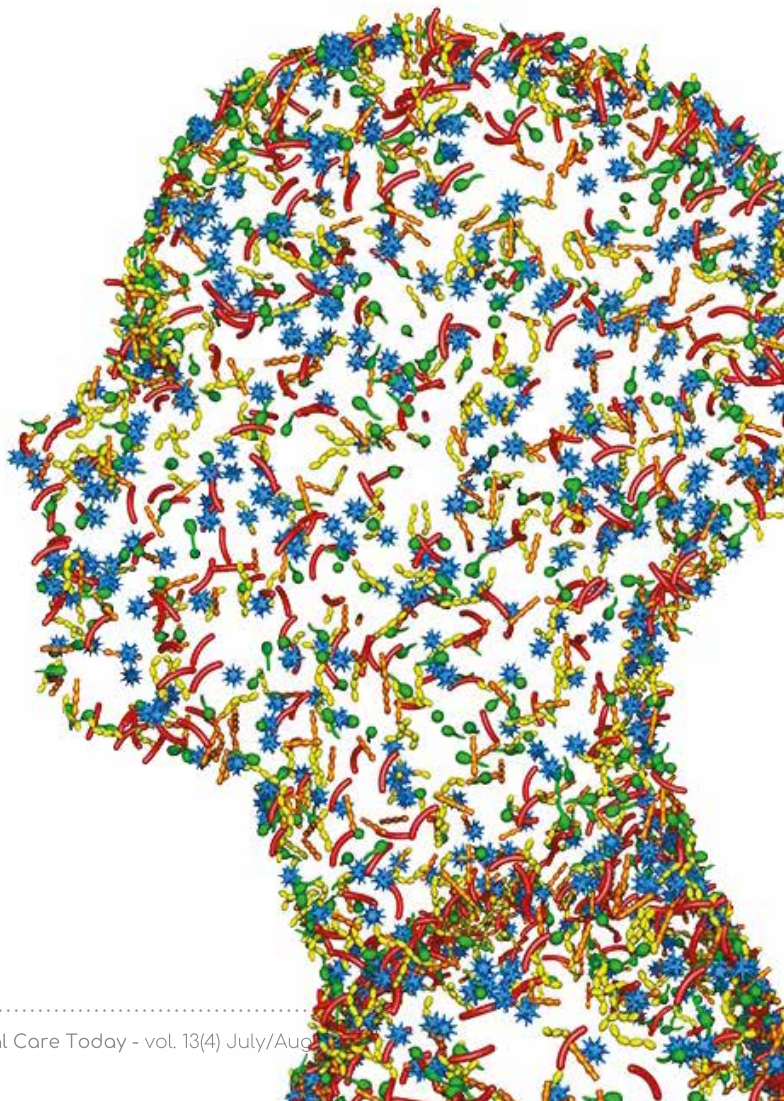
Cosmetic interference with the facial's microbiota is a very difficult topic. In developed countries, we cannot make a proper statement about the "normal" condition, as we all use more or less harsh cleansing products for daily body care which, in my opinion, prevents establishment of the individual "normal" microflora. Human skin was designed to be washed with water and to face the wind and weather and, over millions of years, the perfect microflora co-evolved. So, how can we judge what is right or wrong in today's environment?

The 16S RNA sequencing technologies enable us to identify almost every single species of microorganisms settling on the skin as well as making quantitative predictions about their abundance. We can express this with the Shannon index. However, it is not always a benefit to have such detailed information, as it naturally raises a lot of questions: by comparing the skin microbiome of a set of people, we easily see that there is a huge variation on the occurrence and amount of microbial species on the skin. Who can tell which species is the right one and which is the wrong one? What is the reason for the big variability? We can assume that this might be already determined shortly after birth, when the newborn's skin is "infected" with the microbiota of the mother, which surely has a big impact on the earliest establishment of this important shield against pathogenic intruders. But what comes next? How does the microbiota develop? What are the trigger factors? Nutrition, hormonal state, stress level, cleansing routines, cosmetics, the climate zone, seasons, working outside or in an office, meeting friends – you name it. All might have an effect on the skin microbiota. Up to now, no bacterial strain was identified as aggravating normal skin ageing. In certain conditions of impure skin, it might be of relevance to shift the skin microbiota in a more biodiverse condition, as sebum overproduction will fuel the establishment of a monoculture of e.g. *Propionibacterium acnes*. However, it will be extremely challenging to prove that only this will have a benefit for impure skin as the skin microbiome is not stable and by that it is hard to perform long term studies.

Consumers are aware of the terms pro-biotic and pre-biotic as claimed by the food industry. I have the

impression that consumers looking for healthy food and try to take care for their body are aware of the possibilities which the food industry can offer. However, the terms pro- and pre-biotic seem claims, which sound very good but are not well understood. Who can tell the difference between both terms off the top of their head?

I think there are great opportunities by working on the microbiota in terms of claiming a higher biodiversity, which can be an appreciated parallel to nature's biodiversity, which we all want to preserve. However, on the side of efficacy claims for facial care, more research has to be done and we are now only at the very beginning.



FROM SCIENTIFIC DISCOVERIES TO CONSUMERS' EXPECTATIONS: WHAT'S NEW ABOUT SKIN MICROBIOTA?

Pauline Rouaud-Tinguely, SILAB

The skin is the site of many microbial communities. The number of studies aiming at analyzing interactions between the skin and its microbiota has increased considerably in recent years, making this subject a scientific breakthrough.

SURPRISING MOTHER NATURE

In parallel, recent studies have shown that plants also host numerous microorganisms in their roots, their flowers and even in their floral nectar. This latter is an important resource of nutrients sugars, amino acids, proteins and secondary metabolites for pollinators but also for the microorganisms they introduce inside. This particular composition makes the floral nectar a microhabitat whose physicochemical characteristics selectively filter groups of microorganisms such as yeasts. Among them, *Metschnikowia reukaufii* is considered to be dominant and specific to floral nectars thanks to its adaptogenic metabolism. Furthermore, it is a genuine regulator of the nectar microbiota.

Hence by drawing inspiration from nature, its customized sampling in the floral nectar of the emblematic and refined porcelain flower *Hoya carnosa* opens a new era to innovative biomimetic cosmetic concepts. Indeed, it shows that we can isolate microorganisms that regulate the plants' ecosystems and use them as natural raw materials to extract and purify active molecules that in turn, regulate the skin's ecosystem.

SKIN MICROBIOTA IN AGED SKIN

Indeed, it is known that a finely regulated community of "good bacteria" on the surface of the skin is responsible for immunity, nutrition and defense against aggressions by pathogens. This

symbiosis between the skin and its microbiota is therefore beneficial and essential for its beauty. Unfortunately, in some conditions, this fragile equilibrium can be ruptured, thus leading to the appearance of dermatological disorders.

Although the microbiota of these pathological skin has been largely studied, very few data are available on the modulation of microbiota on healthy skin. To this end, the 16S rRNA gene sequencing technology and the associated downstream bioinformatics processing pipelines are perfectly suitable to compare the abundance of bacterial communities between different body sites or groups of volunteers and under different stressful conditions.

For instance, the specialists of SILAB's microbiota platform proved for the first time in dermo-cosmetic research that the skin microbiota of Caucasian women is disturbed across aging, with an increase of the opportunistic *Corynebacterium*.

CURRENT COSMETIC SOLUTIONS

Currently, the cosmetic market offers prebiotics, probiotics or antibacterial products. Nevertheless, the microbiota can be apprehended through the biological way, thanks to natural molecules able to restore endogenous immune and mechanical barriers in order to rebalance the skin microbiota.

Anyways, before rebalancing skin microbiota, it is essential to perform *in vivo* modeling studies in order to decrypt the potential imbalances in the skin microbiota under stress conditions or during aging.

As today's consumers have been educated on the beneficial effects of bacteria and the importance of preserving this flora to maintain a beautiful skin, the emergence of new concept regarding microbiota will be well-accepted by the cosmetic market.



UNDERSTANDING SKIN MICROBIOME : SCIENCE VERSUS CONSUMERS

Marisa Meloni, VitroScreen

HOW CAN THE GERMS ON FACIAL SKIN BE QUANTITATIVELY AND QUALITATIVELY ANALYSED AND COMPARED BETWEEN DIFFERENT SUBJECTS?

The best technique to identify all the bacteria on skin consists in a genomic approach based on the identification of the total microbiota members by the 16S sequencing.

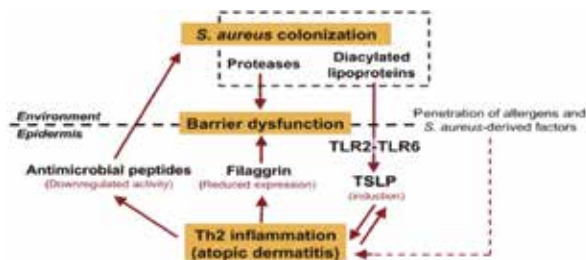
This technique allows to identify all the bacteria present on the skin surface and their relative abundance, without any bias due to the non-cultivability of several bacterial species, that cannot be cultivated in laboratory conditions but that inhabit the human skin, even in high quantities. Our individual microbiome derives from the one that has been inherited from our mother at birth and it continuously evolves during the first years and infancy and cannot be considered mature in the adult because during the aging process it is modified as well.

CAN A SPECIFIC MICROBIOME BE ASSOCIATED TO HEALTHY SKIN OR DISEASES SUCH AS ATOPIC DERMATITIS?

Generally speaking, microbiome can prevent and/or have positive effects on many type of diseases. "Healthy skin" is often described as presenting a balanced microbiome; however, this definition is not precise: to reach a better skin health (wellness) could be also a status in which microbiome contributes thanks to the maintain of microbiome biodiversity.

Dermatological Literature shows an increasing number of papers on the relationship between an unbalanced microbiome and AD. The predominance of *Staphylococcus aureus* and its biofilm phenotype is responsible for atopic

flares (an acute worsening of the disease). *S. aureus* triggers keratinocytes to produce Thymic Stromal Lymphopietin (TSLP), a fundamental biomarker for AD. The predominance in AD patients of *S.aureus* is a clear example of microbiota unbalance in presence of a impaired barrier that creates a vicious cycle: *S aureus*-derived TLR2-TLR6 ligands and extracellular proteases promote AD. In turn, the inflammatory TH2 cytokine milieu in patients with AD further promotes the *S aureus* colonization.



The vicious cycle between colonization by *S.aureus* and AD. J.Allergy Clin Immunol 2010; 126:985-93

HOW CAN COSMETIC PRODUCTS AND/OR INGREDIENTS HELP?

Regarding AD, cosmetics can really help at different levels: by enhancing the barrier function and thus counteracting the *S.aureus* adhesion; by rebalancing the microbiome, acting selectively on *S.aureus*

and by enhancing the *S.epidermidis* role and associated benefits (production and expression on natural antimicrobial defence proteins as β defensins). However, there are very few brands that have adopted a direct communication such as "targeting your skin microbiome". There is anyhow an increasing interest and curiosity of the consumers to understand the differences in probiotics, prebiotics and also postbiotics and their effects on skin.

DO THE CONSUMERS REALLY UNDERSTAND THESE CONCEPTS, DO THEY IN LARGE NUMBERS ADHERE TO SUCH CLAIMS AND BUY PRODUCTS BASED ON THEM?

Despite the increasing scientific evidences of the importance of the skin microbiome, the awareness of the EU consumers about the benefits generated by its protection or modifications is at a very early stage. Consumers are rather interested in gut microbiome and benefits associated to the use of probiotics. A very interesting communication challenge is now open in particular within consumers like the "millennials" or "greens" who are demonstrating a "microbiome friendly" approach.

MICROBIOME QUORUM SENSING MODULATION. A GENUINE MECHANISM OF ACTION TO REBALANCE THE SKIN MICROBIOTA DYSBIOSIS

Oscar Exposito, Vytrus Biotech

MICROBIOME AND SKIN

There is a layer of microorganisms on top of our skin, that is typically stable, but hormonal imbalances, stress or pollution can cause an excess of sebum that ends up in

an imbalance of different key microbial players, among them:

- *Propionibacterium acnes*
- *Staphylococcus aureus*
- *Staphylococcus epidermidis*

The microbial dysbiosis has a key role in acne formation, which has a direct effect on the general appearance of the skin. ...but why does this imbalance in the microbiome

happen? And how can it be controlled?

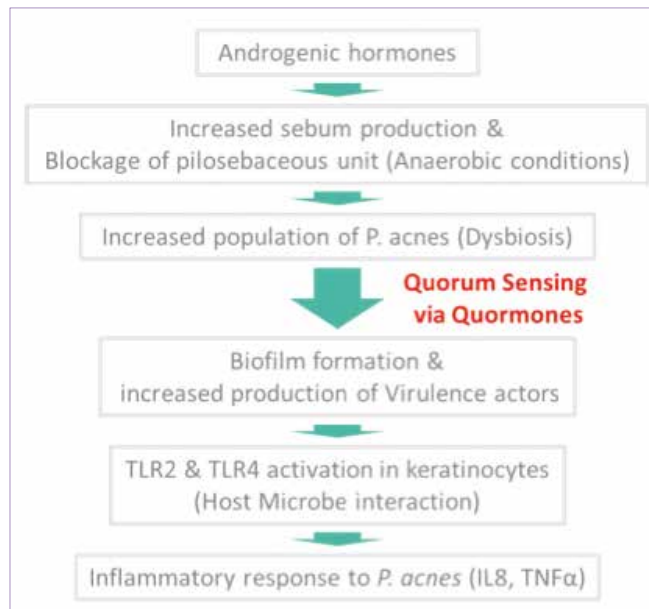
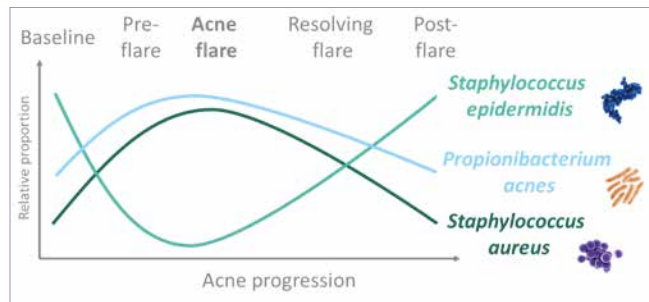
Currently acne is treated with seborregulators, chemical peels and antibiotics but the recurrence of acne is still increasing. The excessive use of antibiotics in acne generates the problem of the generation of resistance. Also, when the microbiome is not virulent, it doesn't have a negative effect on the skin, and some species are beneficial for it, so a bactericidal substance is not the best option to treat the condition. Nowadays, lots of active producers are working towards solving these microbiome imbalances, through different strategies, developing new mechanisms of action and at the same time helping improve the general appearance of the skin.

QUORUM SENSING

Microorganisms communicate with each other with a system called Quorum Sensing, which is done through volatile bio-chemicals called QUORMONES AutoInducers (AIs), synthesized and secreted by bacteria that diffuse away into the surroundings. The neighboring bacteria "sense" the local density of these Quormones via QS Receptors

Bacteria form biofilms which are self-structured and complex communities of microorganisms, that constitute a protection system and that are related to the virulent form of many microbes. Like in all communities, a coordinated communication system is crucial, and bacteria use Quorum Sensing for it. The exchange of these small molecules enables bacteria to sense how many other bacteria are nearby and to communicate with them. When they reach a certain threshold population (or quorum), the expression program of the bacteria changes in unison, and they start doing group behaviors. Through Quorum Sensing, bacteria determine whether to compete, collaborate or simply coexist with each other, and it allows them to respond rapidly to changes in the environment.

The human skin microbiome plays an important role in skin beauty, health and disease. Microbial biofilms are a critical element in acne, and Quorum Sensing has a key role within microbe-microbe & human-microbe interactions.



The microbiome layer on our skin communicates internally and with the keratinocytes by exchanging Quorum Sensing signals. Quorum Sensing regulates the microbiome **virulence: when there are environmental changes (e.g. excess of sebum due to hormones), bacteria detect them**, and there is a dysbiosis (impaired microbiota). Then Quorum Sensing is activated among them, and since their numbers have passed the threshold, there is a call to release virulence factors, forming bacterial biofilms, that ultimately cause skin disease.

Virulence happens because bacteria speak with each other by using Quorum Sensing, but if they couldn't sense the signals, they wouldn't form biofilms. Hacking their communications offers a new mechanism of action for beauty ingredients and products, and is the key to avoid this virulence, offering an extremely good alternative to the use of antibiotics.

PROTECTION FROM PLANTS

Plants also have a microbial layer that can also be beneficial or virulent. They are constantly attacked by microorganisms and have designed a genuine and smart system to fight against them, called Quorum Quenching, that uses Anti-Quormones.

VYTRUS BIOTECH has developed a product that uses these Plant Anti-Quorum Sensing signals, that disarm the bacteria by hacking their communication systems, just like plants do. The approach of Quorum Sensing inhibition by using Anti-Quormones generates much less possibilities for the generation of microbial resistance because the bacteria is not killed or threatened (bacteriostatic approach).

Morinda Citrifolia Callus Culture Lysate is a concentrated metabolome of totipotent cells from Noni (*Morinda citrifolia*), rich in anti-quorum sensing molecules (Anti-Quormones) specially designed for "dermohacking": to act synergistically against Quorum Sensing mediated microbial dysbiosis while perfecting the skin appearance. It blocks the microbiome communication signals to avoid the formation of biofilms and the development of virulence, without killing or threatening the microbiota. ■

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