WHITEPAPER

The Skin Microbiome
in health and disease

Understanding the science
behind Skin Microbiome.

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CONTENTS

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AN INTRODUCTION TO THE SKIN MICROBIOME

The Skin Microbiome is a relatively new term to most people.

Indeed, even in the scientific and medical world it has only really been studied in the last few decades[1]. This paper aims to show what the Skin Microbiome is, what it is made up of, how it affects our skin and whole-body health and why it has become such a hot topic in recent years.

We will look at the history of the microbiome and how the discovery of and research into the skin microbiome is helping to change how we protect our skin health.

We will look at what makes up the skin microbiome, discovering how different bacteria, fungi and viruses live on the skin and what their importance is in keeping skin healthy. We will examine diseased skin, and what causes the changes in an individual's skin microbiome.

We will examine how skincare and cosmetics companies are teaching their customers about the skin microbiome through advertising and marketing. We will look at how companies are also investing in research and product testing to discover the best products for a balanced human skin microbiome.

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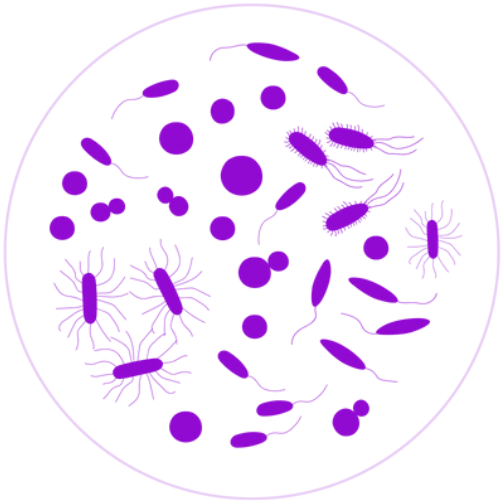
Finally, we will look at what the future holds for skin microbiome research, the investments being made for future discoveries, how to nurture the skin microbiome and the new technologies that will help us understand the skin microbiome space.



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The number of people with an identical skin microbiome. Just like fingerprints!

80

Approximate number of fungi species identified in the skin microbiome.

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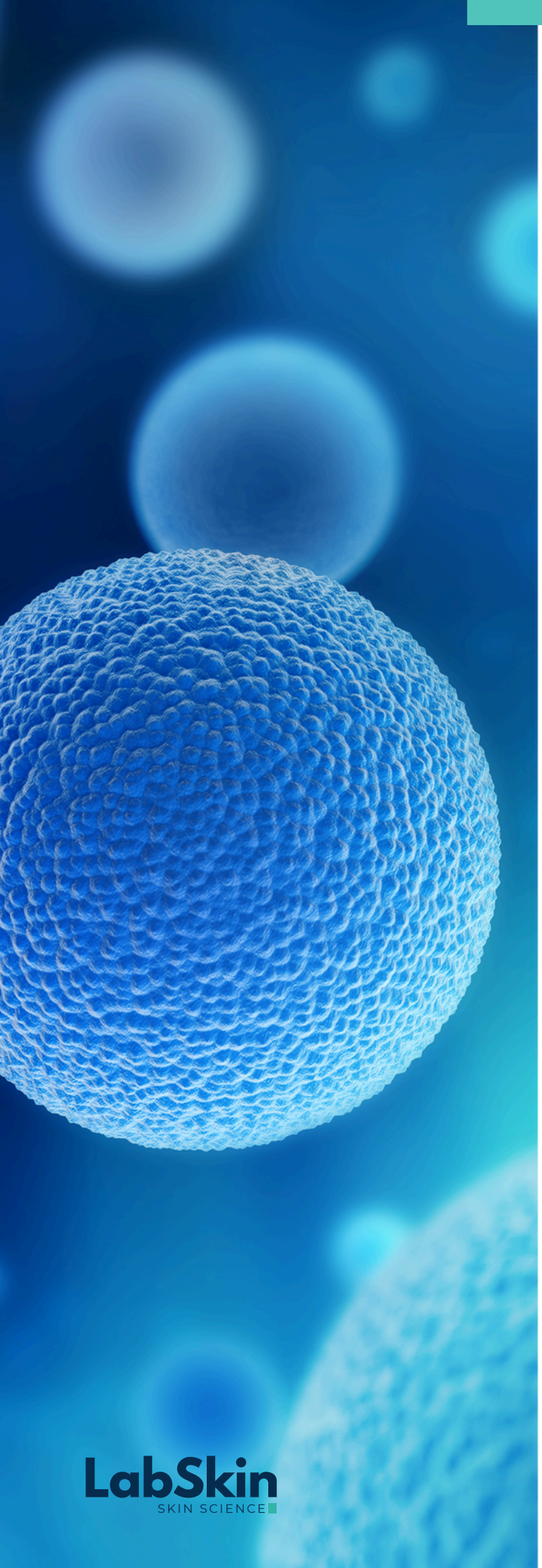

WHAT IS THE SKIN MICROBIOME?

The skin microbiota is the term used to describe the millions of different organisms – bacteria, viruses and fungi – that live on Human Skin.

The skin microbiome is the genetic material of all these microbes.

The skin is the human body's second largest organ in terms of surface area, second only to the intestines. It contains seven layers of tissue and guards muscles, bones, ligaments and internal organs.

There are over 1,000 species of bacteria and up to 80 different fungi specie on skin that have been identified, with research ongoing[2]. Some of these species are already familiar as they are also present in our gut microbiome and include Staphylococci, Streptococci and Candida

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species. Most skin microbiomes are found in the outermost superficial layers of the epidermis and at the site of hair follicles. It is estimated that over 1 billion bacteria inhabit a single square centimetre of skin[3].

THE HISTORY OF SKIN MICROBIOME RESEARCH

The first scientific evidence that microorganisms exist as part of the normal human system emerged in the mid 1880's when Austrian paediatrician Theodor Escherich found a type of bacteria in the intestinal flora of healthy children and children who suffered with a diarrhoeal disease[4]. The bacteria was later named Escherichia Coli, more commonly known as E. coli.

In subsequent decades scientists discovered further bacteria in oral, digestive and urinary systems. Research in characterising human microbiota continued throughout the 20th century and began to incorporate the skin microbiome by mid-century[5]. However, the tools and procedures used for studying the skin microbiome were culture-based and only capable of studying bacteria under certain growth conditions.

As technology has progressed, so have the capabilities available to researchers in the field of the skin microbiome. New molecular techniques developed to identify and quantify the bacteria have changed the way we view the microbial world. Genomic-based approaches to characterising skin bacteria have revealed a much greater diversity in organisms than a purely culture-based approach ever could[6].

1000

Approximate number of identified bacteria in the skin microbiome.

1 billion

The number of bacteria living on 1 square cm of skin.

WHAT DOES THE SKIN MICROBIOME DO?

The skin microbiome is as individual to each person as a fingerprint.

No two people can have the same microbiome as lifestyles, diet, location, ethnicity etc. all play a part in the make-up of the skin microbiome. Even the microbiome of an individual is different on various parts of their own body such as arm-pits, face, hands and feet[7]. This is due to many factors such as weather exposure, heat, sweat production, work environment etc. In addition, it is well known that age plays a factor in the skin microbiome. Children have different skin microbiome to teenagers and different again to adults, which can be seen in the increase in acne during puberty, for example[8]. The microbiome of a newborn will depend on the type of delivery - vaginal microbes being found on natural deliveries and stomach microbes being found on babies delivered by cesarean section[9].

The thought of all these bacteria living on the skin might seem abhorrent to some, however the bacteria work in the same way as the well understood and documented impact of "good" bacteria that live in the gut. The "good" bacteria on the skin work as protectors from external bacteria that attack and harm it. The more diverse the "good" bacteria are the better they work[10].

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The skin microbiome also helps to fight infection[11]. The skin microbiota is adapted to the acidic skin environment but also influences the ecological conditions around it to enhance the healing process. The same as "good" gut bacteria - it works by overcrowding the "bad" bacteria, preventing it from growing.

Skin conditions such as eczema, acne, and rosacea are believed to be connected to a lack of diversity in the skin microbiome. Recent studies have shown for example, that individuals with eczema have a microbiome not found in individuals without[12].

Society's obsession with cleaning and hygiene - while obviously one of the key advancements in modern history and, of course, vital for survival – has also led to massive changes in the skin microbiome and harsher conditions for it to thrive on[13]. All the above skin conditions, as well as others, have seen an increased number of people reporting symptoms.

SKIN MICROBIOME AND SKIN DISEASE

The microbiome of normal human skin is highly diverse and varies considerably from individual to individual.

This creates difficulties when trying to understand and treat skin disease, as each sufferer has different microbiome make-up and no two treatments will have the same outcome.

Advances in technology have allowed researchers to begin examining diseased skin in greater detail than was previously possible. Acne, psoriasis, eczema and dermatitis are probably the most well-known and most common examples of skin disease, although there are many more[14]. There are numerous studies available regarding these diseases, however treatments and outcomes vary so

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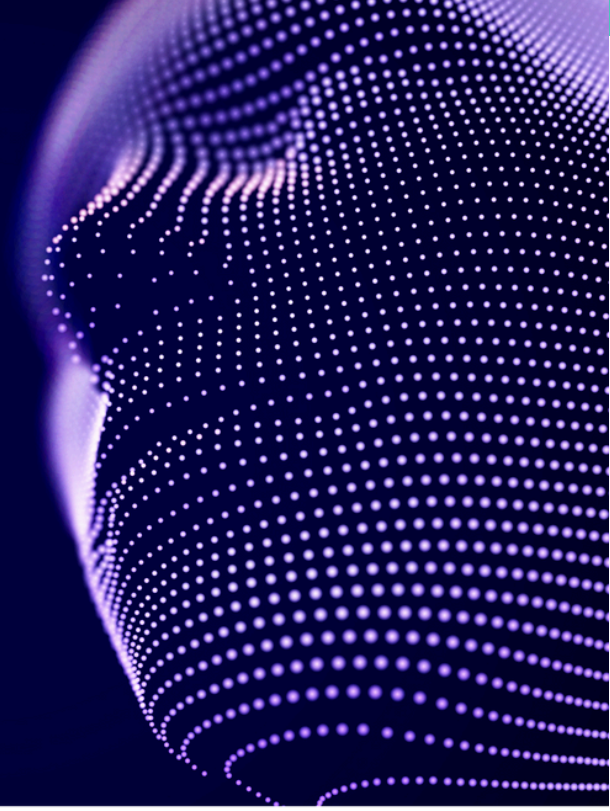
much that a lot more study is required.

All skin disease is believed to be intrinsically connected to the human microbiome. The "Brain-Gut-Skin Axis" is an interesting theory and one in which more research is required for the "Skin" element[15]. The background to the theory is that emotions (depression, stress, anxiety etc.) can cause changes in the gut microbiome which are then transported to the skin microbiome – acne flares, psoriasis flares, etc. all link back to whatever signals are being activated in the brain.

The biggest barrier to treating skin disease such as psoriasis or dermatitis is in developing new drugs or topical treatments. The cost alone to develop new drugs is estimated to be over $2.6billion[16], with many drugs not even making it to market due to the cost involved. Testing on human skin is difficult, with many variables involved and clinical testing of human volunteers being unreliable[17]. Researchers and drug development companies now understand that an alternative testing solution is required to ensure continued advancements in skin disease treatments. Technologies now exist that can enhance and speed up the development of new treatments.

SKIN MICROBIOME AND TECHNOLOGY ADVANCEMENTS



Genomic sequencing, artificial intelligence and other developments

From the early 20th century, safety and efficacy testing on drugs, cosmetics and skincare products involved using animals to perform initial tests before advancing to next stage human clinical trials. The idea was to ensure any reactions caused by ingredients of a product would be highlighted before trialling on humans.

Towards the latter part of the 20th century animal rights group began protesting against this practise and over the ensuing decades have worked towards animal cruelty for cosmetic and skincare products being diminished and eventually banned outright. This is certainly the case in the EU since 2013[18], with the US FDA continuing to work with individual states to bring a ban into place[19] and China changing its cosmetics and skincare testing rules at the beginning of 2020[20]. Many other countries in South America and the Far East have also adapted their rules and laws or are in the process of doing so.

While this is a welcome change for the world, it has also generated new challenges for the world of skincare. With the jump in skin microbiome research has also come a requirement for new products to come to the

SKIN MICROBIOME AND THE SKINCARE MARKET

The recent introduction of the term “skin microbiome” to consumers has created a new business opportunity for the skincare and cosmetic industry.

The current combined global market is valued at around $450 billion and is expected to grow another 20% by 2024[21].

Large brands are now partnering with academics and research companies to discover new ways to treat skin conditions and new product formulations that will work in harmony with the skin microbiome, answering demand from health-conscious consumers.

Before now, manufacturers worked from the base formulation that defines their brand and make new additions or remove certain ingredients from formulations to

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create “new and improved” products without the need for costly product testing and regulatory approval. For new products aimed to benefit the skin microbiome, new claims must now be made and backed up with efficacy and safety tests.

25%

North American share of the cosmetics market worldwide.

37%

Make-up share of the cosmetic market worldwide.

20.12m USD

Forecasted market value growth of skin care worldwide.

The awareness of the human microbiome in the consumer psyche has progressed in the last decade from a basic understanding of how it works, to the health-conscious consumer demanding products that work in harmony with their microbiome, be that gut-health or skin-health.

Following on from this, there is now an understanding among leading brands that new products must be formulated for this growing market. There are two big challenges facing manufacturers: the sheer amount of data available to them to wade through and the constant knowledge-gathering that is occurring in the relatively immature skin microbiome research domain.

A solution is needed to ensure all the information available is collated to ensure time is not lost during new product development. The cost of new product development also needs to be kept as low as possible. Critically, new products must comply with regulatory standards required to prove safety and efficacy.

THE FUTURE OF SKIN MICROBIOME

As the skin microbiome space is still so young in terms of research, there are many different topics to be discussed in the future. Further study on the “Brain, Gut, Skin Axis” will help to develop skincare and cosmetics products that will not only be used to look good, but also to promote whole body health and not be just “skin-deep”.

Research also continues into wound healing through the skin microbiome; understanding how the skin microbiome assists or hinders the healing process to enable reduction of the risk of bacterial infections such as MRSA. Life-long diseases such as diabetes come with the risk of wound lesions and slow wound repair. Further investigation into the skin microbiome on these lesions may help future treatments to help prevent spread of gangrene, for example.

Utilising artificial intelligence diagnostic tools with the vast amount of data being gathered has the potential to discover the susceptibility of an individual to a certain diseases such as diabetes, Crohn's, psoriasis etc. The potential could be there to take a swab from the skin to examine markers that match a disease and work towards early diagnosis and better treatments.

The development of human skin equivalent models has helped the withdrawal of animal testing for cosmetics and skincare products in many countries. Having human skin equivalents that can host bacteria, fungi and viruses is a massive technological breakthrough – instead of having to test on multiples of people, a small number can now be swabbed and their data cloned to replicate multiple test subjects.

LABSKIN 3D SKIN MODEL FOR TESTING THE SKIN MICROBIOME

Labskin researchers and scientists have worked tirelessly over the last decade to develop a commercial lab-grown, full-thickness human skin equivalent that can mimic human skin and assists in determining the impact of cosmetics and skincare products on the skin's microbiome. While similar living skin equivalents have existed for decades, Labskin's 3D model is the first with the capability of colonising skin microflora, meaning the most accurate results from tests without the need for animal testing or expensive and time-consuming human trials.

Labskin makes this technology available to both commercial and research institutions and encourages working together on projects to advance the knowledge of how the skin microbiome works. Labskin AI technology gives the capabilities to create a repository of data and predictive analysis related to skin, supporting industry and academia in the creation of rapid and ethical discoveries and strategies for new products and medical advancements.

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