AN INTRODUCTION TO

THE SCALP MICROBIOME

Understanding the science behind
the scalp microbiome
A whitepaper by Labskin.

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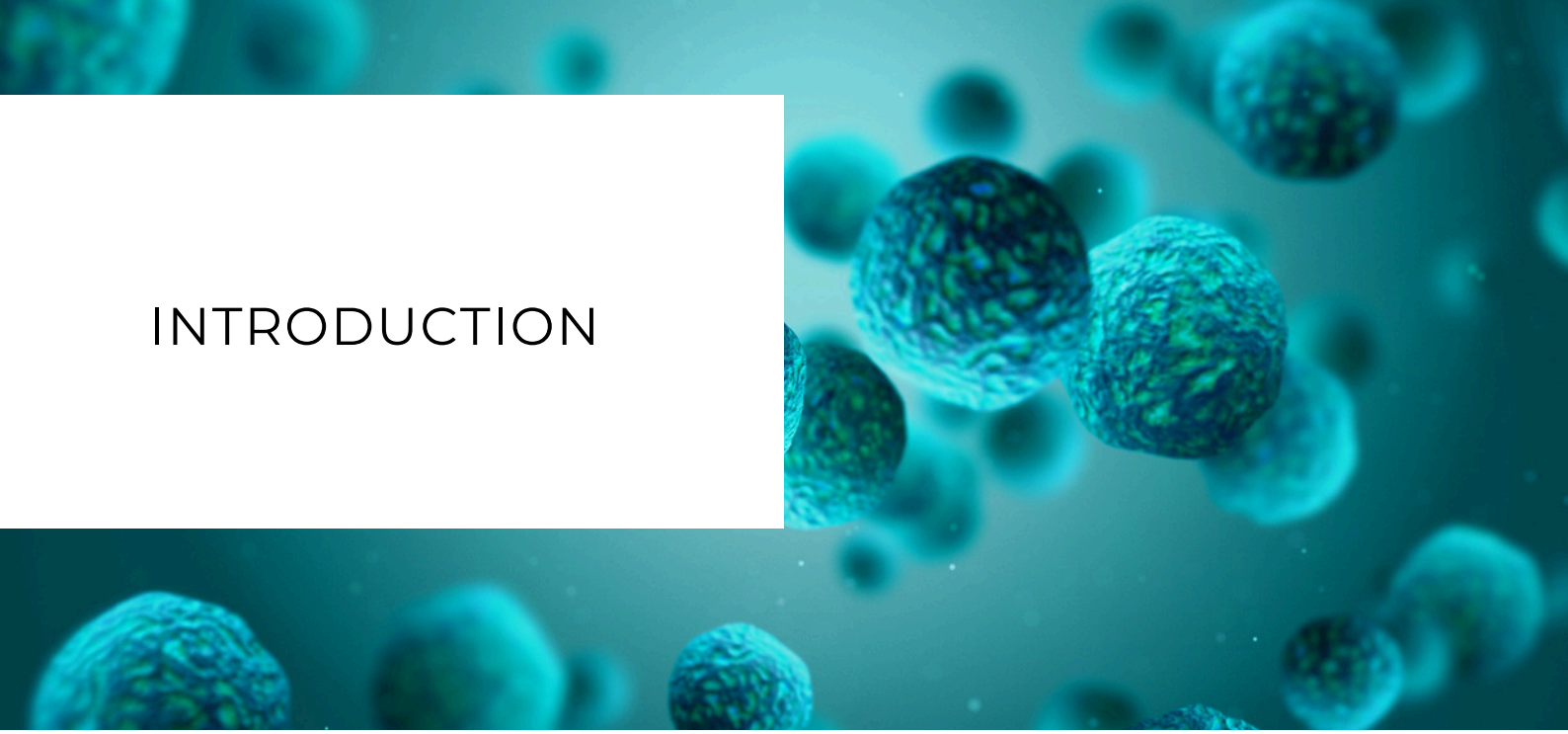

INTRODUCTION

Analysis of the scalp microbiome and the microbiota that colonise this ecosystem is growing rapidly.

Research institutes, academics, and global cosmetic companies are exploring the world of the scalp microbiome. Evidence increasingly shows that an imbalance of scalp microbiota can be associated with infections, inflammatory disorders, and other scalp ailments. [1]

The main objective of this paper is to explain what the scalp microbiome is, explore the microorganisms that inhabit the scalp and hair follicles, and learn how the microbiota can be linked to common scalp disorders.

Research of the scalp microbiome is still in its infancy compared to other microbiomes of the body, much is unknown of how it controls, regulates, and affects functions of the scalp.

However, innovative analytical technologies are accelerating the pace of knowledge gathered on individual scalp microorganisms, and in turn, opening up new opportunities for scalp and hair-care markets.

With the advent of human skin equivalent (HSE) models that mimic the scalp microbiome and eliminate the need for animal testing, the demand for scalp microbiome friendly products can be met at a much faster rate.

Looking to the future of scalp microbiome research, new and existing products and ingredients can be analysed at a much lower cost, clinically proven as safe and effective, and recognised globally with microbiome friendly certification.

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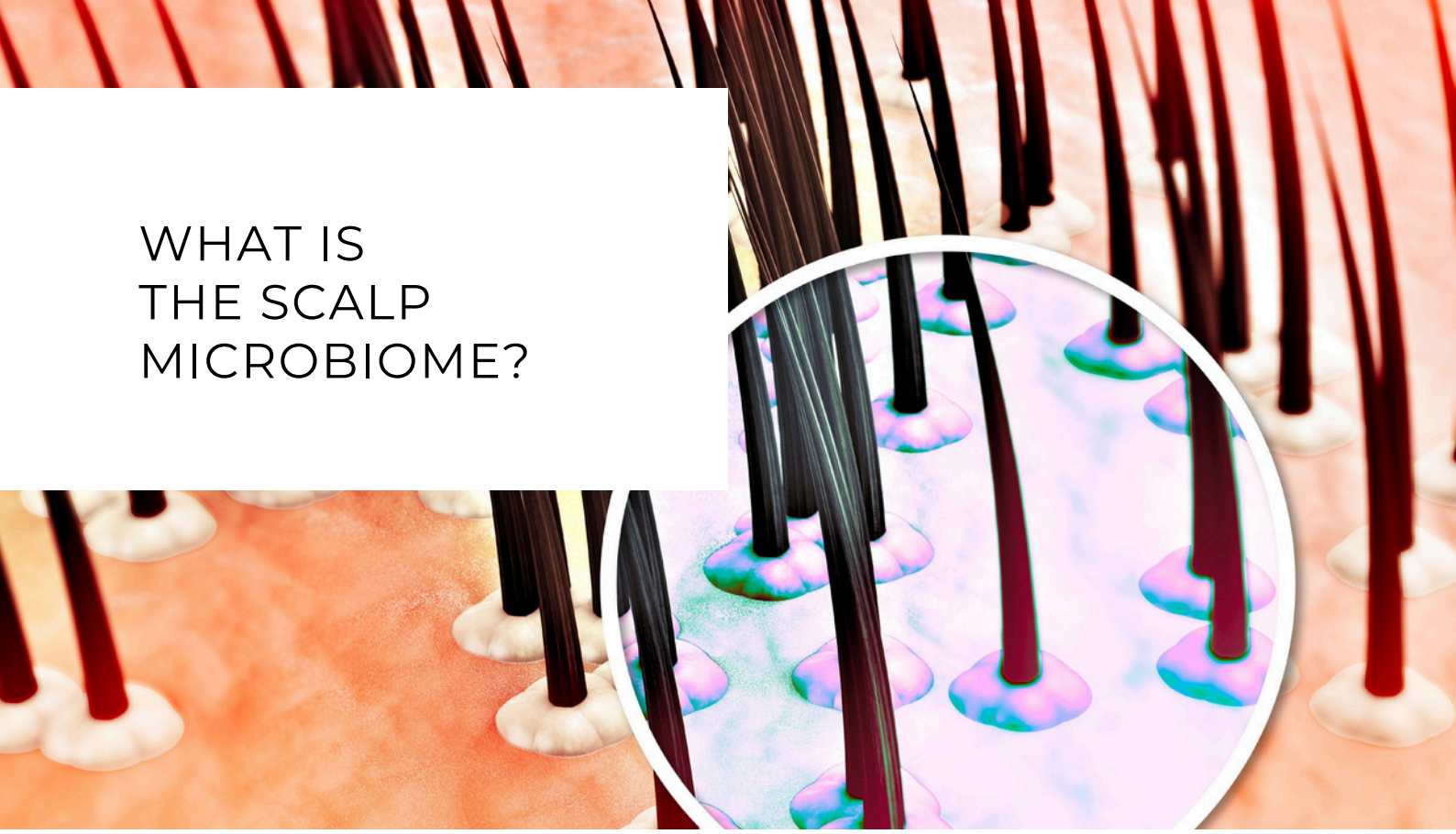

WHAT IS THE SCALP MICROBIOME?

Your scalp microbiome consists of a diverse mix of bacteria, fungi, viruses, parasites, other microorganisms and their genes.

Regarded as the first line of defence against invading pathogens, [2] the scalp microbiome, along with individual hair follicle microbiomes, work together to create a balanced ecosystem. When dysbiosis, an imbalance of the microbiome occurs, common scalp conditions such as dandruff and other inflammatory disorders can arise. [3]

Unlike the skin and gut microbiomes, which are predisposed to bacteria, the scalp microbiome harbor a higher number of yeasts, particularly the *Malassezia* species, [4] including:

- *M. restricta*
- *M. globosa*
- *M. furfur*

Other uncultured species of *Malassezia* have been identified on the scalp [5], along with a variety of bacteria [6] that can create a healthy scalp environment or contribute to the development of cosmetic, dermatological, and auto-immune scalp disorders. These include:

- *Cutibacterium acnes*
- *Corynebacterium* spp.
- *Staphylococcus* spp.

Similar to other microbiomes of the body, composition can be related to pH levels, temperature, moisture, and sebum content. Therefore, every individual has a unique set of microorganisms colonising their scalp.

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THE HISTORY OF SCALP MICROBIOME RESEARCH

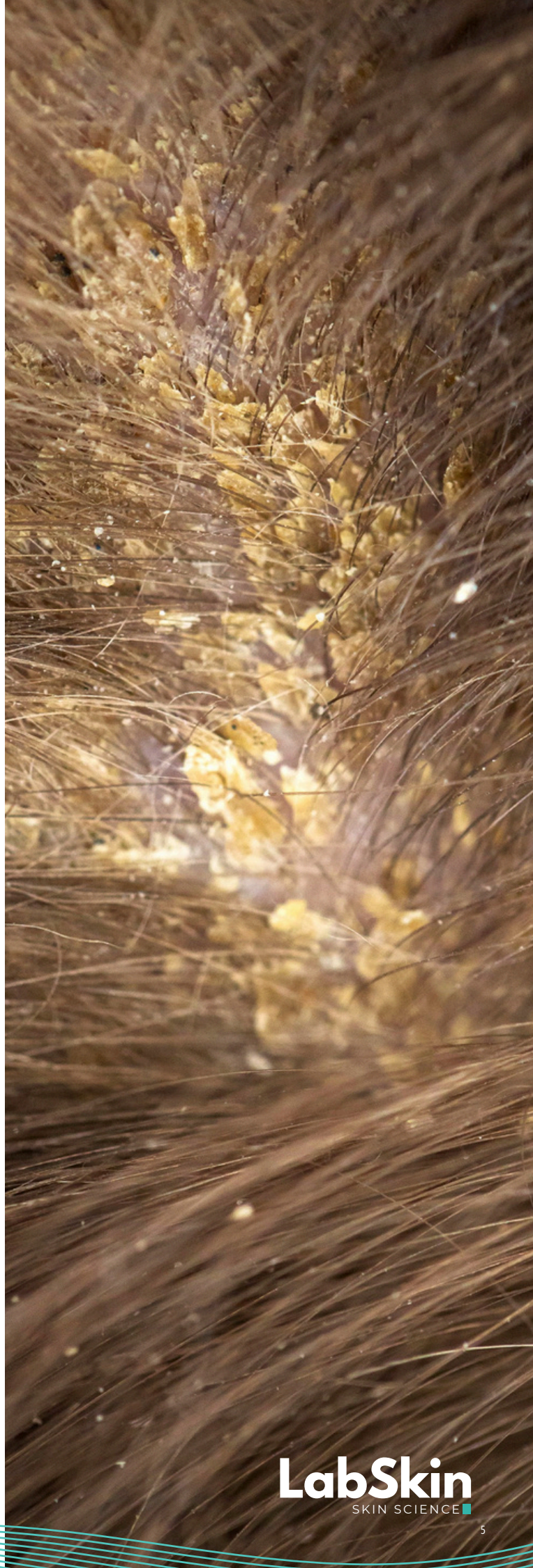
First documented studies of the scalp microbiome are less than 20 years old.

Research into the scalp microbiome continues to gain pace, however at a much slower rate compared to other microbiomes of the body.
Though the volume of studies has been underwhelming, the application of next-generation sequencing [7] and associated data analysis has deepened our understanding of the subject.

In recent years, studies have shown associations between an imbalance of the scalp microbiome and common scalp disorders, such as:

- Seborrheic dermatitis [8]
- Pruritus
- Dandruff
- Alopecia areata (AA)

While there is still much to learn regarding the functionality and structural aspects of the scalp microbiome, metagenomics has paved the way for deeper analysis of this ecosystem. [9]
By studying communities of the scalp, potential causative factors for the above-mentioned scalp disorderscan now be explored.



WHAT DOES THE SCALP MICROBIOME DO?

Shielding the scalp from infections and irritations, the scalp microbiome plays a pivotal role in keeping your hair and scalp healthy. [10] It also affects functions of the scalp such as:

- Hair follicle regeneration [11]
- Sebum production [12]
- Pathogenesis of scalp disorders [13]
- Immune cell maturation [14]

Hair follicle regeneration:

Hair follicles are integral to many functions, particularly thermal insulation and sebaceous dispersion. [15] An imbalance of scalp microbiota can be associated with inflammation and permanent hair loss. Furthermore, studies have shown regeneration relies on a healthy, balanced microbiome, [16] along with the intensive cooperation of epithelial and hair-inductive mesenchymal components. [15]

Sebum production:

Many factors affect sebum production, including age, hormones, lifestyle, UV light, diet, and stress. Scalp sebum contains a mixture of cholesterol, triglycerides (TGs), diglycerides (DGs), free fatty acids, and squalene. [17] When an imbalance of the microbiome occurs, sebum production can be affected, inflammatory diseases become more prominent, and have been associated with the progression of androgenetic alopecia (AGA). [18]

Pathogenesis of scalp disorders:

An imbalance of the scalp microbiome can be associated with the onset and progression of multiple scalp disorders. For instance, dandruff scalps are associated with an overabundance of *Staphylococcus* spp. and *Malassezia restricta*, [19] while a higher proportion of *Corynebacterium* spp. has been found on the scalps of severe alopecia areata (AA) patients. [20]

Immune cell maturation:

Depending on penetration depth and composition of hair follicle microbiota, direct interaction of bacteria with immune cells can produce a local immune response. Ultimately, this may contribute to acute and chronic scalp inflammatory disorders, and may interfere with immune cell maturation in deeper hair follicular compartments such as the dermal papilla (DP) and dermal sheath (DS). [21]

SCALP MICROBIOME AND SCALP DISORDERS

Age, lifestyle, geographic location, genetics, and other factors all contribute to scalp disorders.

Research into the treatment of various scalp disorders is accelerating, but there's still a lot to learn when it comes to determining causative factors. An imbalance or overabundance of certain microorganisms have been linked to individual disorders. With this information, technological advancement in metagenomics and next-generation sequencing opens a door for therapeutic products that balance the scalp microbiome.

Seborrheic dermatitis

Seborrheic dermatitis (SD), considered a chronic form of eczema, has a global prevalence in 11% of the population. [22] Interestingly, it is predominant in those with white skin and a higher body fat content. Recent studies indicate the cause is an inflammatory reaction to an imbalance of the scalp microbiome. Potential fungal biomarkers observed in one particular study are *Malassezia* spp. and *Aspergillus* spp., while potential bacterial biomarkers are *Staphylococcus* spp. and *Pseudomonas* spp.. [23]

Scalp pruritus

Scalp pruritus, generally recognised as an itchy scalp, is an easy to diagnose but difficult to treat scalp disorder. Investigations are exploring an imbalance of the microbiome as a cause, as studies have shown differences in the microbial communities of itchy and non-itchy parts of the scalp. [24] For example, *Lactobacillus*, *Morganella*, and *Pseudomonas* species have been found in itchy regions of the scalp,

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indicating that restoring balance with microbiota-targeted treatments can be achieved.

Dandruff

Dandruff affects up to 50% of the global population. [25] Characterised by scaly patches and itchy skin, it is linked to a combined interaction between the scalp microbiome, sebum composition, and host susceptibility. While most studies focus on an overabundance of fungal species, most noticeably *Malassezia restricta*, [26] higher incidences of *Staphylococcus* spp. can also be found. Anti-fungal shampoos are often the go to treatment for dandruff. However, studies indicate that maintaining an equilibrium between the fungal and bacterial microbiota would be far more effective. [27]

Alopecia areata

With a lifetime incidence risk of higher than 2%, alopecia areata (AA) is estimated to affect 1 in 1000 of the population across the globe. [28] Classified as a non-scarring autoimmune hair disorder, causative factors have yet to be clinically determined. Studies have found an increase in Actinomycetota and a decrease in Bacillota, while higher levels of *Staphylococcus* and *Cutibacterium* species have been found in the scalps of AA patients. [29] *Prevotella copri*, a bacterium relevant to the pathogenesis of rheumatoid arthritis, has also been identified in subepidermal compartments of AA scalps. Indicating that therapeutic treatments that focus on the immune system may be beneficial for the management of AA.

ADVANCES IN TECHNOLOGY ALLOWS GREATER INSIGHTS INTO THE SCALP MICROBIOME

New therapeutic approaches for scalp disorders develop as technology advances.

Offering higher sensitivity, resolution, and a more comprehensive analysis of the scalp microbiome, “omics” techniques are used to identify the genomic community inhabiting the scalp and hair follicle ecosystems. With the ability to assess functionality of the microbiome, [30] common “omics” techniques used for analysis of the scalp microbiome include:

- Metagenomics
- Metabolomics
- Transcriptomics
- Metataxonomics
- Proteomics

In the development of scalp disorder treatments, determining the efficacy of a product includes assessing changes in the scalp microbiome after use. To avoid the controversial method of colonising human scalps with microbes, without enough safety data

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from preclinical studies, a far more ethical approach can be achieved with human skin equivalent (HSE) technology.

Mimicking the scalp microbiome in a laboratory setting allows for physiological and environmental exposures to be assessed in a safe manner. Comprehensive and reproducible analysis can take place using various other technologies, such as:

- Next generation sequencing (NGS) [31]
- Polymerase chain reaction(PCR) technology [32]
- Amplicon-based NGS [33]

Determining the cause of microbial imbalances is vital for the discovery of new therapeutic treatments for scalp disorders. With this knowledge in hand, microbiome friendly products can be targeted towards individual ailments, and create new avenues for income in the scalp and hair-care markets.

SCALP AND HAIR-CARE PRODUCT MARKETS

Increasing demand for scalp microbiome friendly products

As consumers deal with the physical and psychological effects of scalp disorders on a daily basis, there is a never-ending search for products that actually work. Globally, the hair and scalp care markets are expected to reach $121.4 billion by 2027, indicating a market growth of 6.5% CAGR during this period. [34]

A higher awareness of environmental factors and the effects on hair and scalp disorders is driving market growth. Increasingly, personalised or customised products are offered to meet consumer demand. Not only for scalp disorders, but to address more common concerns with the hair, including:

- Frizz control
- Colour retention
- Cleansing
- Softening
- Strengthening
- Scalp care
- Moisturisation

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Harsh chemicals are found in the majority of scalp and hair care products, [35] but awareness of the importance of a balanced scalp microbiome is beginning to alter consumer decision making. Due to the lack of scalp microbiome models available, most hair and scalp products don't factor the microbiome into the equation. As it stands, we are yet to fully understand the cosmetic and dermatological impact of many ingredients, including:

- Colourants
- Surfactants
- Actives
- Preservatives
- Emollients
- Texture ingredients

By introducing human skin equivalent (HSE) models to test the impact of ingredients on the scalp microbiome, a more comprehensive assessment of said ingredients can take place. From a financial perspective, R&D costs are dramatically reduced with a HSE model, as clinical trial participant numbers can be halved. [36] All while bringing new products to market that meet safety, regulatory, and efficacy standards at a much faster rate. [37]

FUTURE OF SCALP MICROBIOME UNDERSTANDING

Compared to the skin and gut, research of the scalp microbiome is still in its infancy. However, as technology advances and scalp microbiome models become more readily available, new avenues for personalised hair and scalp care treatments can be explored.

Consumers are beginning to have greater awareness of how natural ingredients impact skin and scalp health, [38] and aim to avoid contact with chemicals of emerging concern (CECs). Proving claims of safety and efficacy, while preventing an imbalance of the scalp microbiome is becoming more important than ever. Eventually, hair and scalp products designed to prevent or treat common scalp disorders will lead the market.

Access to scalp microbiome testing will become more readily available to consumers. Subsequently, the gathered data will accelerate understanding of how the scalp microbiome is associated with scalp ailments, leading to more targeted solutions for consumers.

As the scalp microbiome movement grows, the hair care industry and regulators are exploring ways to validate microbiome friendly claims, using a variety of novel in vitro and in vivo methods. Global cosmetic companies including Unilever, L'Oréal, and L'Occitane are leading the way by assessing and marketing products in this manner.

LABSKIN: A 3D MODEL FOR TESTING THE SCALP MICROBIOME

Eliminating the need for cosmetic testing on animals, Labskin has developed a lab-grown, full-thickness human skin equivalent (HSE) model that mimics the scalp microbiome. With this model, it's easy to determine the impact of any product ingredient on the microbiota that inhabit the scalp.

While similar HSE models do exist, Labskin is the first commercially available model with the capability of colonising the scalp microbiota. [39] Clinical trial participant numbers, financial burdens, and product development time are dramatically reduced by utilising its reproducible and robust data generating performance to replicate multiple test subjects.

Commercial clients and research institutions are working together to grow a repository of scalp microbiome data using Labskin's platform, predictive analysis, and AI technology. Hair and scalp-care clients can then use this optimum real-world environment to test new and existing ingredients, clinically prove safety and efficacy claims, and gain a world-recognised microbiome friendly certification. [40]

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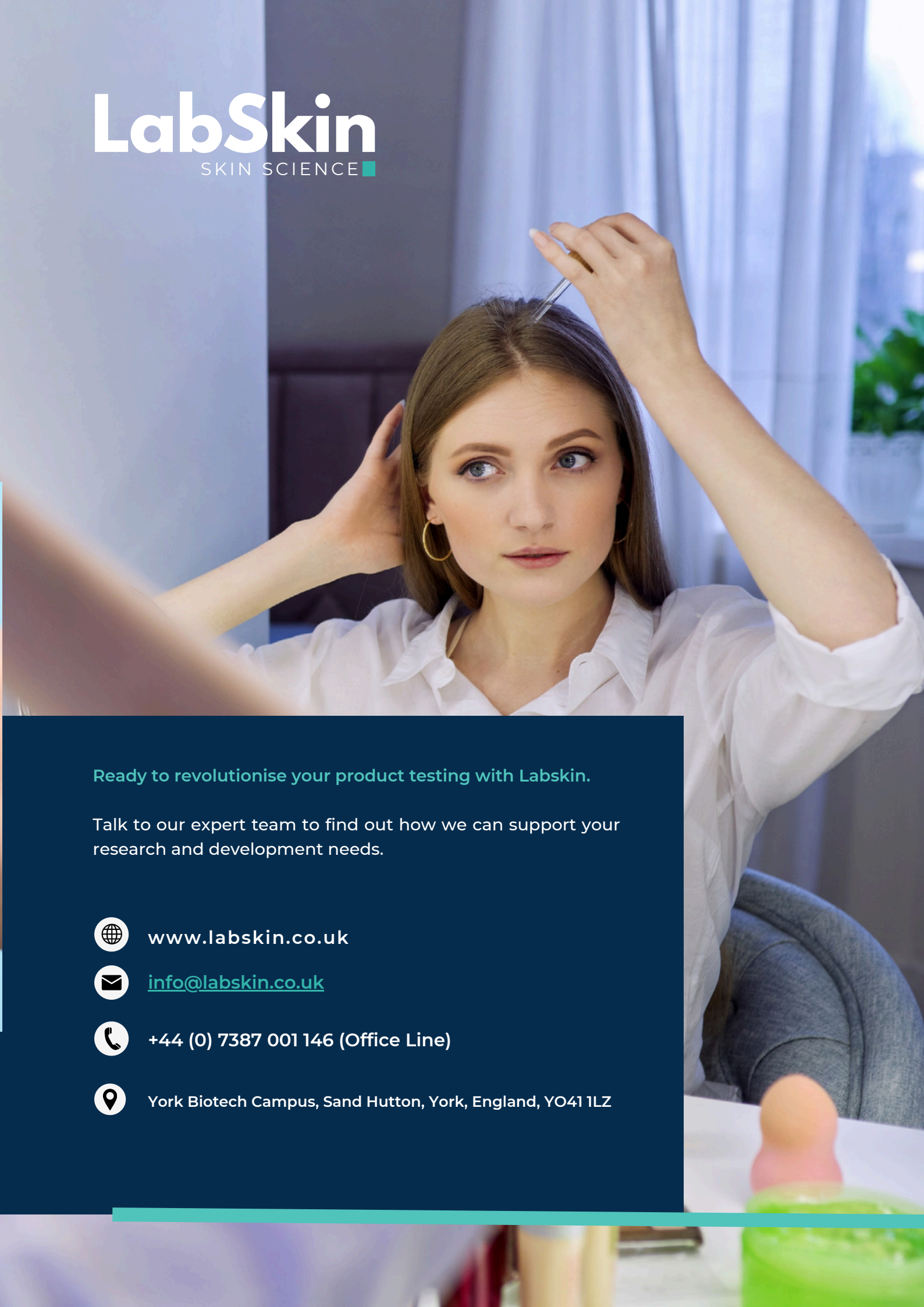

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