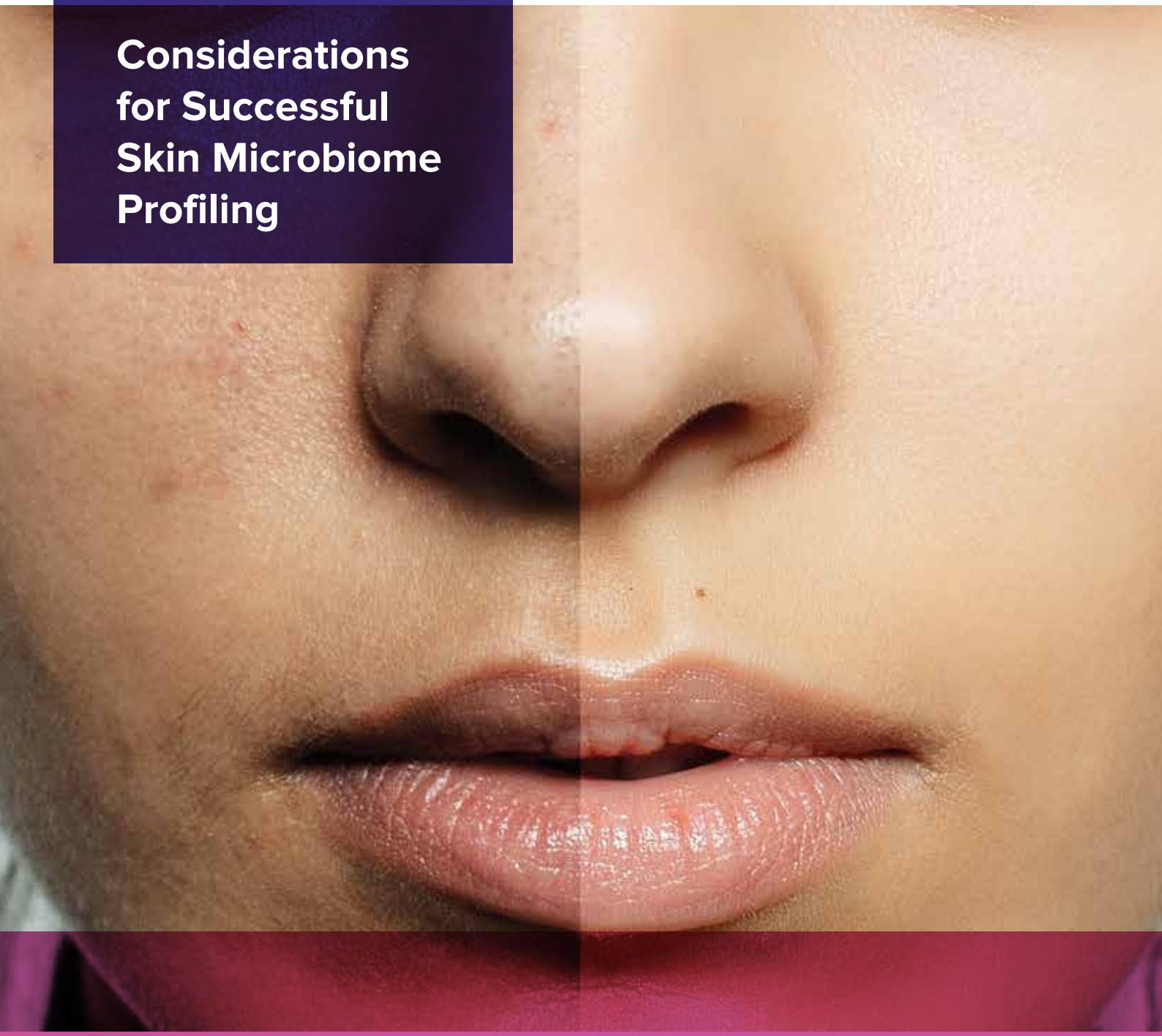
THE TOP 3

Bio-Me
Microbiome Profiling

Considerations for Successful Skin Microbiome Profiling



Bio-Me AS

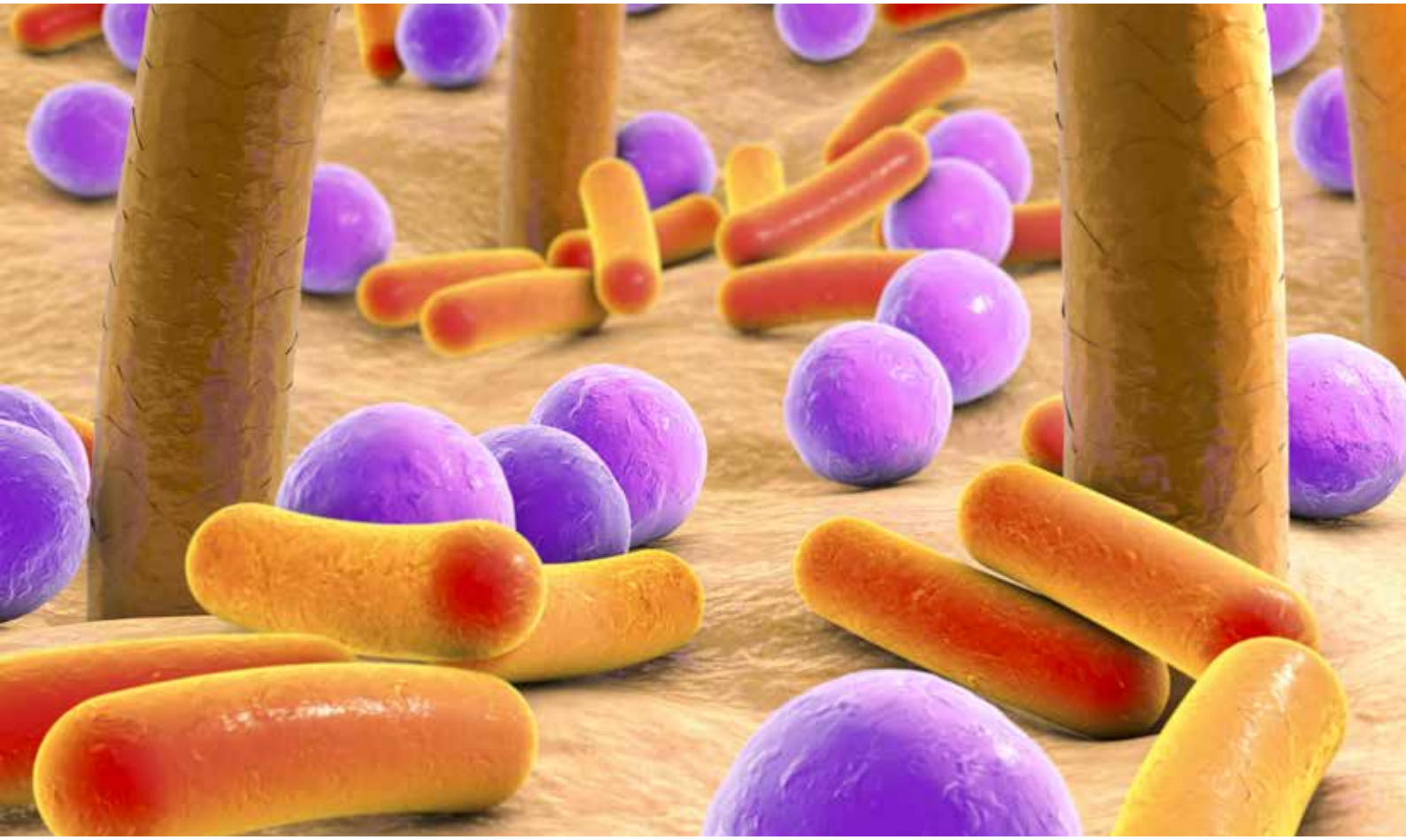
Oslo, Norway

Introduction

The human skin is colonized by millions of microbes (i.e., bacteria, fungi, and viruses)[1] that, together with their genetic information, constitutes the skin microbiome.

The study of the human skin microbiome – which has become a cornerstone in the cosmetic and dermatological fields[2] – is broadening our understanding of skin health and disease and facilitating the development of topical pre/pro/postbiotics and live biotherapeutic products (LBPs) for different skin conditions.

Most skin microbiome studies currently use next-generation sequencing (NGS) approaches, specifically amplicon sequencing and shotgun metagenomics[3]. In this report, we will go through three key factors to consider when using skin microbiome profiling tools.



The Top 3 Considerations for Successful Skin Microbiome Profiling

1. Resolution

Amplicon sequencing is the most common strategy to characterize cutaneous microbial communities. While this method has key strengths, such as its cost-effectiveness, it is usually limited to genus-level resolution[4]. A recent breakthrough in NGS platforms has been the development of long-read technologies, such as Oxford Nanopore. While full-length 16S rRNA gene amplicon sequencing has shown to give a better resolution at the species level than short-read technologies[5], long-read platforms tend to have lower per base accuracy, higher total costs, and lower throughput[6,7].

Shotgun metagenomics, which is increasingly used in skin microbiome profiling, allows for taxonomic identification at species and even strain level[2]. This high resolution is relevant when strains within a species harbor different gene content that determines functional differences[1]. For example, *C. acnes* strains have different pathogenic potential[8]. However, the "price" for the increased resolution of shotgun metagenomics is higher sequencing costs and more complex data analysis[9]. These become more relevant issues as the number of samples analyzed increases – for example, when profiling a high number of trial participants, monitoring probiotics/LBP engraftment on the skin, performing quality control of probiotics/LBP production runs, or assessing the effect of a skin product over time.

2. Host DNA and biomass

Amplicon sequencing, targeting the bacterial 16S rRNA gene and the fungal ITS1 region, can be used in samples containing host DNA[10]. As mentioned above, such an approach is generally only able to provide genus-level information.

Although shotgun metagenomics can provide important species and subspecies resolution, its use is challenging in skin samples. It requires a high starting amount of DNA[11], which may pose a challenge for skin samples, which have a low microbial biomass[12]. In addition, skin samples contain high levels of host DNA, where it can represent more than 90% of the total extracted DNA[3]. Therefore, although host DNA sequences can be removed later during data processing, a large part of the reads have already been "spent" on sequencing the human genome. This results in increased costs due to the deep sequencing runs required to yield relevant information. The depletion of host DNA is another way to reduce human reads from shotgun metagenomics and consequently decrease sequencing costs. However, different host DNA-depletion approaches have shown taxonomic biases[13].

3. Absolute Quantification

As NGS instruments have a fixed capacity (number of slots to fill), the data obtained for all detected taxa will be described as relative abundances (which are mutually dependent).
This poses a challenge, as the use of relative abundances can lead to misleading results[14] (Figure 1).

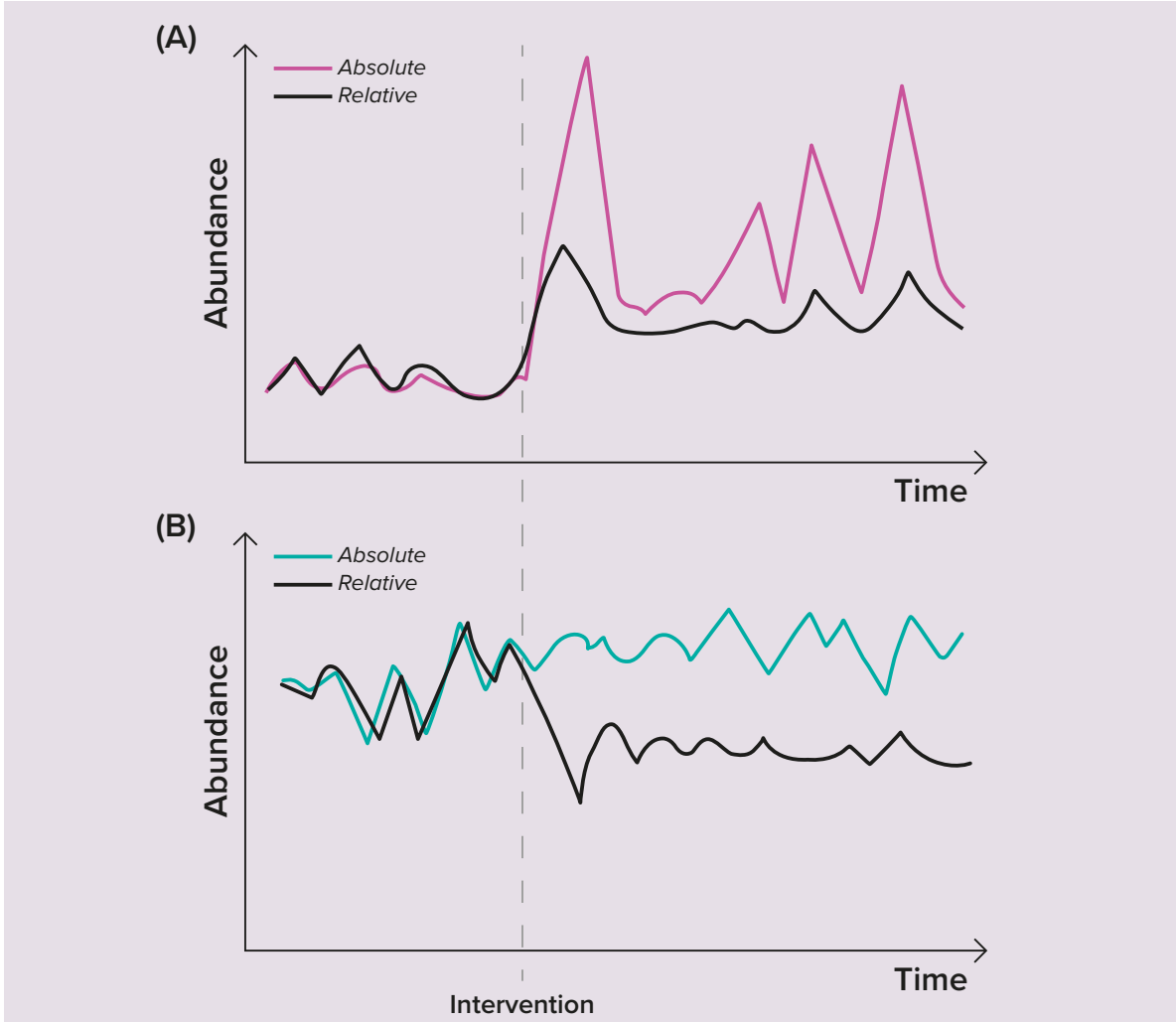


Figure 1. The use of relative abundance can produce false positives. (A) The abundance of a taxon is increased after an intervention (pink line). This increase is also reflected in its relative abundance (black line). (B) Another taxon is not influenced by the intervention (green line). However, the intervention has a negative effect on its relative abundance (black line) due to the increased relative abundance for the taxon in (A). Based on Jian et al.

In addition, the quantification of skin microorganisms is important to address the bioburden of common skin microbes and whether it increases in specific skin disorders[15].

Several approaches allow absolute quantification of microbial taxa, such as qPCR[16]. Different methods have been integrated into NGS pipelines to allow for quantitative data, e.g., exogenous spike-in bacteria[8]. However, they increase the cost and complexity of the data generated and are not yet widely used in the human microbiome field[14].

Transforming Skin Microbiome Analysis with Precision Microbiome Profiling (PMP™)

Bio-Me has developed the **Comprehensive Skin Microbiome Panel** with a precise analysis of **50 key bacterial and fungal targets**. The PMP™ approach is built on a qPCR-based platform delivering accurate information about the microbiome in a high-throughput format. Results are directly actionable – no need for bioinformatics steps for data processing – and produced more rapidly (4 hours of turnaround time for 192 samples) and more cost-effectively than traditional sequencing approaches.

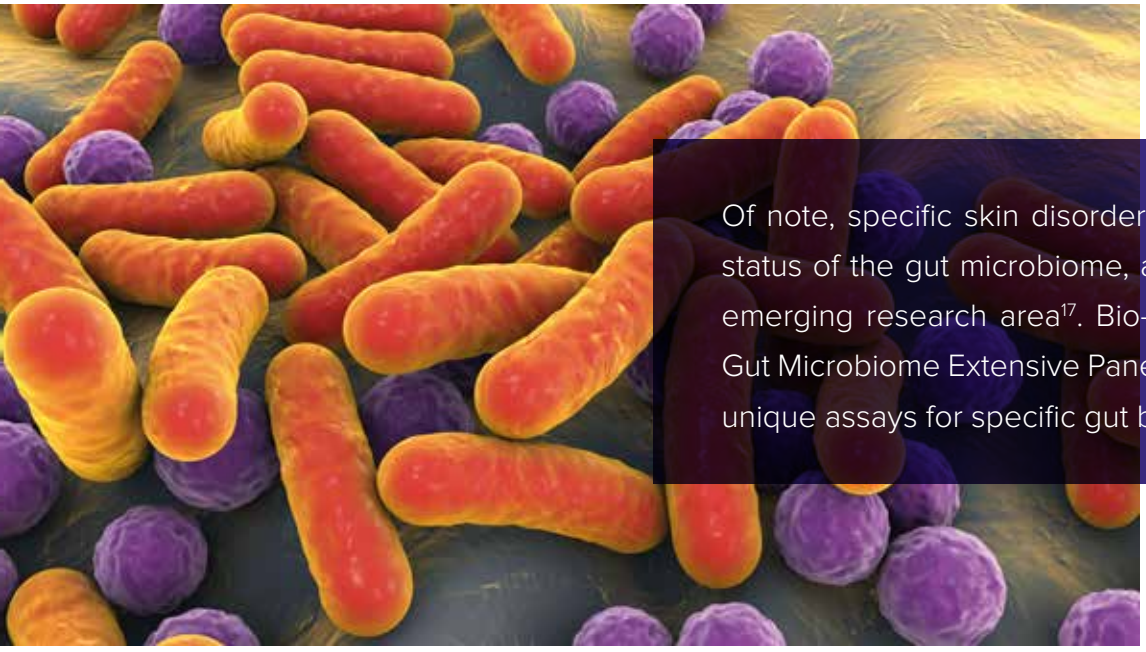
In addition, the Comprehensive Skin Microbiome Panel meets the needs for a skin microbiome profiling tool:

High-level resolution – It provides the same resolution as shotgun metagenomics (down to species and subspecies).

Not impacted by host DNA – The targeted approach used overcomes the challenges associated with a high presence of host DNA in the sample.

Quantitative – It provides the number of genomes per taxa, as well as the relative abundance for the targeted taxa.

Custom proprietary strains assay design upon request.



Of note, specific skin disorders have been linked to the status of the gut microbiome, and the **gut-skin axis** is an emerging research area[17]. Bio-Me has also developed a Gut Microbiome Extensive Panel consisting of close to 100 unique assays for specific gut bacterial and fungal targets.

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About Bio-Me

To learn more about the Comprehensive Skin Microbiome Panel and the (sub)species targeted, as well as our publications and ongoing projects, please contact us: **sales@bio-me.com**

The Bio-Me team holds core expertise in microbiology, molecular biology, and bioinformatics. The company has a history of collaborating with key opinion leaders in the microbiome space and leading academic institutions in Europe and the US. Our partners are, among others, pharma and biotech companies developing next-generation microbiome-modifying drugs. We support their clinical development programs with our expertise and microbiome profiling solutions. Building on the success of PMP™ for the gut microbiome, we are expanding PMP™ to the skin microbiome space in collaboration with KOLs in the field.

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