# BALANCING SKIN MICROBIOME FACT OR FICTION?

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## **OVERVIEW**

- Modern sequencing methods allow investigation of microbial communities on skin.
- Techniques for sequencing DNA have enabled researchers to find the majority of these microbes
- Microbiome: a "newly discovered organ" broadly encompasses the skin's resident microorganisms (bacteria, archaea, fungi, viruses) as well as their genomic content and metabolic byproducts
- The human microbiome consists of about 100 trillion microbial cells, outnumbering human cells 10 to 1
- The microbes are generally non-pathogenic; they exist in harmony and symbiotically with their hosts

#### Human skin represents an ecosystem



stratum corneum

Epidermis



#### MICRO ENVIRONMENTS

- Glabella (also known as the forehead) sebaceous (oily);
- Antecubital fossa (moist);
- Volar forearm (dry); and
- Toe web space (foot).

## SKIN MICROFLORA

- The number of bacteria on an individual's skin remains relatively constant
- bacterial survival and environment
- A high degree of specificity is involved in the adherence of bacteria to epithelial surfaces.

### SKIN MICROFLORA

- Staphylococcus epidermidis is a major inhabitant of the skin, and in some areas it makes up more than 90 percent of the resident aerobic flora.
- Staphylococcus aureus
- Micrococci: *Micrococcus luteus*
- Diphtheroids (Coryneforms) Corynebacterium acnes.
- Streptococci
- Gram-Negative Bacilli: Enterobacter, Klebsiella, Escherichia coli, and Proteus spp

#### PERCEIVED BENEFITS OF GOOD BACTERIA

- Help mitigate signs of ageing due to exposure to UV
- Maintain pH of skin which ensures proper moisture level while discouraging the growth of inhospitable bacteria
- Boost overall immune function
- Promote the skin's own defense mechanism
- Strengthen the skins barrier as a protective shield
- Reduce Redness and inflammation

### DIVERSITY

Skin microbiome varies from person to person due to a combination of various factors, including

- age
- biogeography
- sex
- Cosmetic use
- genetics
- living environment (rural vs urban).
- Within-individual variation is also related to age and environment.

Wilantho A et al (2017) PeerJ. 5:c4084. Lehtimaki J et al. (2017). Sci Rep Nature. 7:45651 Denda M. (2016). Springer. 403-414

#### MICROBIOME IN HEALTH AND DISEASE

- The human microbiome may have a role in auto-immune diseases like diabetes, rheumatoid arthritis, muscular dystrophy, multiple sclerosis, fibromyalgia, and perhaps some cancers.
- A poor mix of microbes in the gut may also aggravate common obesity.
- Since some of the microbes in the human body can modify the production of neurotransmitters known to occur in the brain, it may also relieve schizophrenia, depression, bipolar disorder and other neuro-chemical imbalances.

## SKIN IMMUNE SYSTEM

- The skin is essential organ to protrct from external aggressors
- Crucial immunological role, "skin immune system" (SIS).
- Complex and dynamic immunity; interaction between the external and internal cutaneous compartments.
- Skin microbiota that live in complete harmony with the immune sentinels and contribute to the epithelial barrier reinforcement.
- Under stress, the symbiotic relationship changes into a dysbiotic one resulting in skin disorders.
- Skin microbiota may have either positive or negative influence on the immune system.

•bdallah F et al. (2017) Skin immune landscape inside and outside the organisms. Med of inflam. 5095293

#### Microbiome and skin Immunity



#### BENEFITS OF "BALANCED" MICROBIOME

- Reinforce skin Barrier function, Reduce TEWL
- Play an integral role in the maturation and homeostatic regulation of keratinocytes and host immune networks with systemic implications.
- Provide protection from UV Irradiation
- Anti-inflammatory activity and wound healing
- Anti microbial activity
- Produce organic acids
- Reduce oxidative stress
- Act as bacteriocides

#### **IS SKIN MICROBIOME BALANCED?**

- Normal skin
- Acne
- Psoriasis
- Eczema
- Antibiotic use
- Excessive use of hand sanitizers

#### MEASUREMENT OF SKIN MICROBIOME

- clinical study design,
- skin sample collection and storage
- sample processing
- DNA sequencing,
- control inclusion,
- data analysis

• End point analysis??

#### STUDY DESIGN

- Specify Research Question
- Select Inclusion exclusion criteria
- Define subject population
- Define metadata of interest
- Control potential confounders
- Determine skin preparation

#### SKIN SAMPLE COLLECTION AND STORAGE

- Collect target samples (Consistent method and sites)
- Obtain blank controls
- Collect metadata
- Maintain stable storage



#### SAMPLE PROCESSING AND SEQUENCING

- Extract DNA (Lysis and DNA quality)
- Define PCR primers and conditions for amplicons
- Include blank controls
- Sequence samples (target and blank samples and mock communities)

Cost: ~135/sample

#### ANALYSIS

- Pre process sequences
- Perform OTU and diversity analysis using metadata
- Perform data visualization
- Deposit data
- Interpretation





DESIGN AND COST ESTIMATE REPEATABILITY STUDY

Three overlapping sites Three days in a row Every week for 4 weeks Every Month for a year (seasonal N=10 Sample analysis @ \$135each 30 samples: \$4,050



\$77K (just for analysis)

#### **CONCLUDING REMARKS**

- Skin Microbiome is like a living organ
- Microbiome "balance" of non-diseased skin can be a fallacy
- Good methods are available to study microbiome, but skin clinical study designs need standardization

## Questions?

