

Because you care
about CONSUMERS' HEALTH



**BIOFORTIS
INNOVATION
SERVICES**

□□□□□ < 0.010 □ μg/□ /25g □
□ (IU) < 13 □ □ uf/d/g □ 0.066 ± 0.038 □ < 10 □



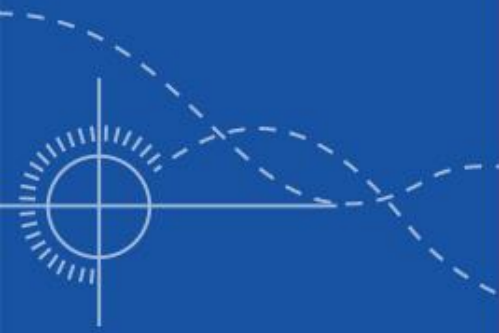
Microbiota Cutaneo, Salute e Bellezza

Alessandra DE MARTINO

Biofortis Mérieux Nutrisciences (Nantes, Francia)

1 Luglio 2016

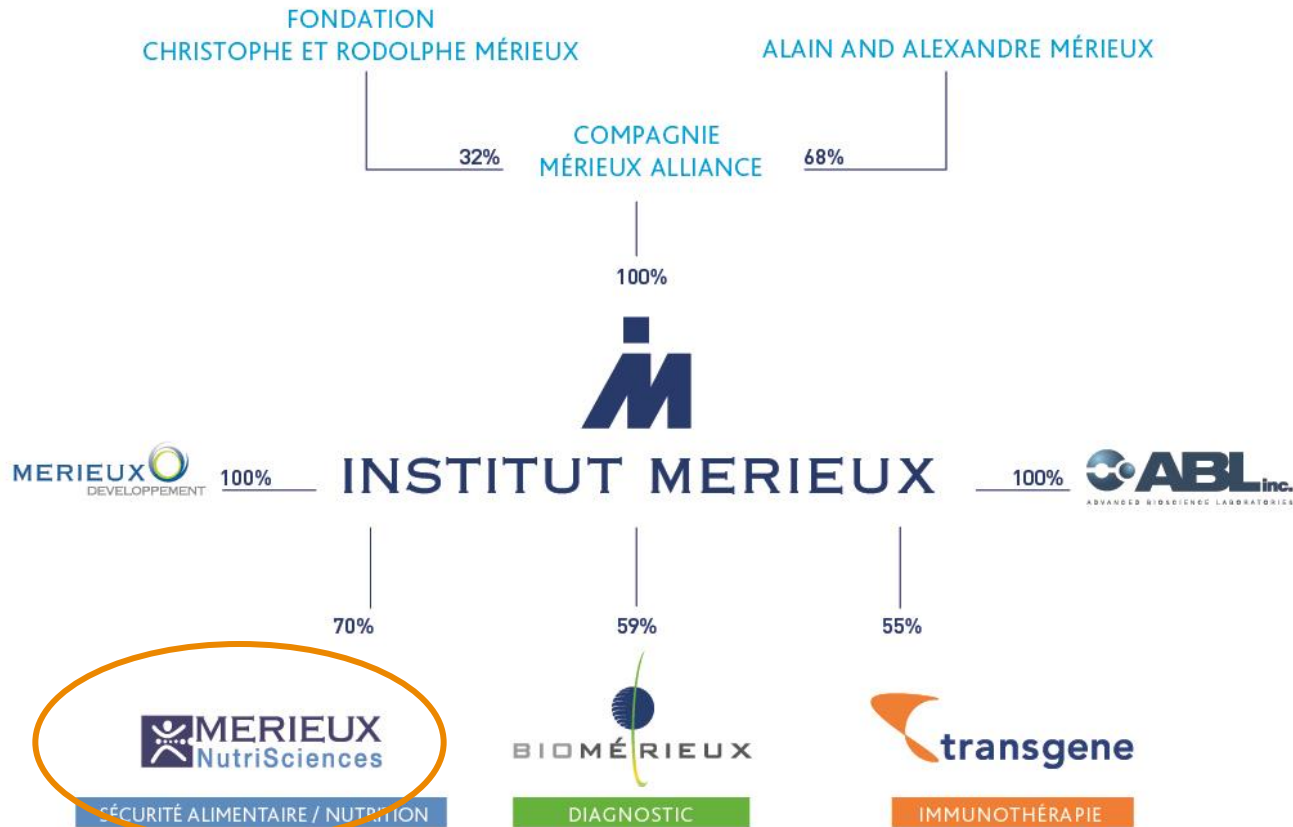




BIOFORTIS WHO WE ARE ?



An Institut Mérieux company

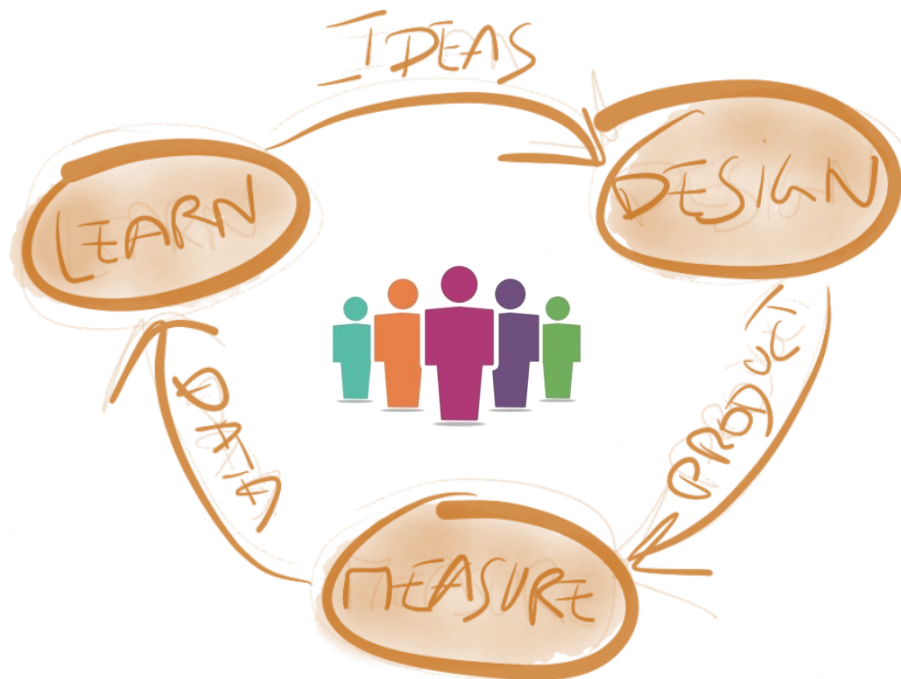


Over 12,000 people committed to global public health
Industrial sites and laboratories in 40 countries
Sales of over 1.8 billion euros



INNOVATION SERVICES





CLINICAL

Health Benefits, Tolerance Studies

SENSORY & CONSUMER

Market Insight and Consumers Tendencies

CONSULTING

Portfolio, Life Cycle, licencing support

RESEARCH

Internal & collaborative R&D projects



- 3 main activities: **CIC**, **Senso labs**, **Analytical Platform**
- >2500 m²
- 65 coll. in Nantes (85 in Fr incl. Paris)
- International R&D Center,

Biofortis dedicated team for each project



Murielle Cazaubiel

Managing Director Europe Sensory + Consumer + Clinical



Strategy and development of project
Isabelle Marx (S&C), Fabrice Richard (Clinical)



BIOFORTIS SENSORY, CONSUMER AND CLINICAL EXPERTS



Virginie Kersulec

Sensory & Consumer manager



Stéphane Deniau

Clinical Manager



Lise Dreyfuss

Sensory & Consumer expert



Alessandra De Martino

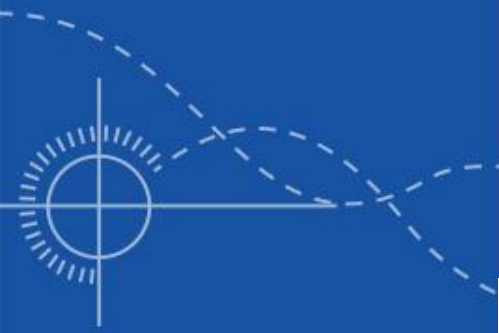
Scientist, Microbiota expert



Sébastien Leuillet

Statistical and data management expert

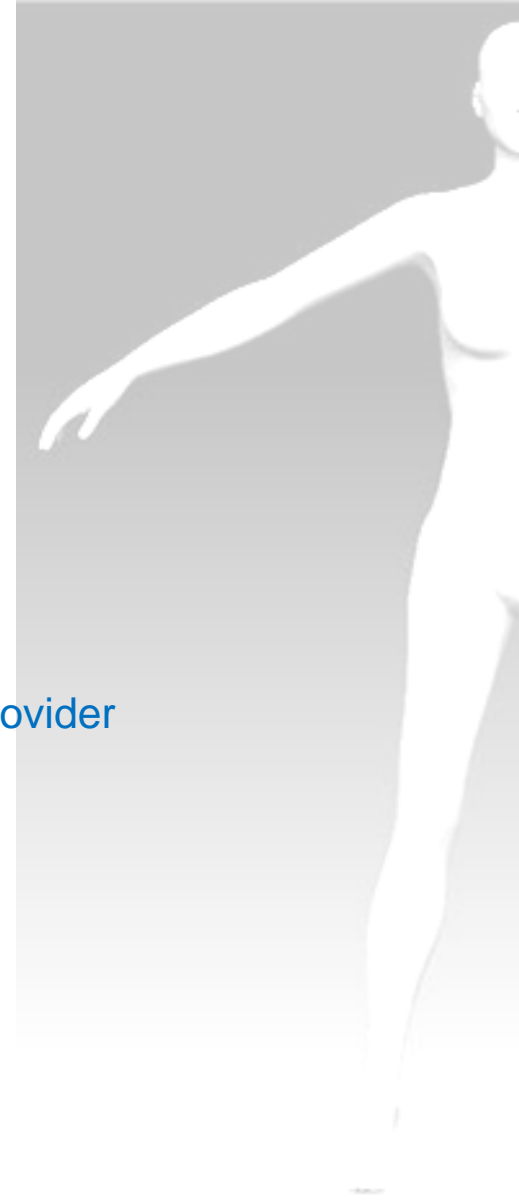
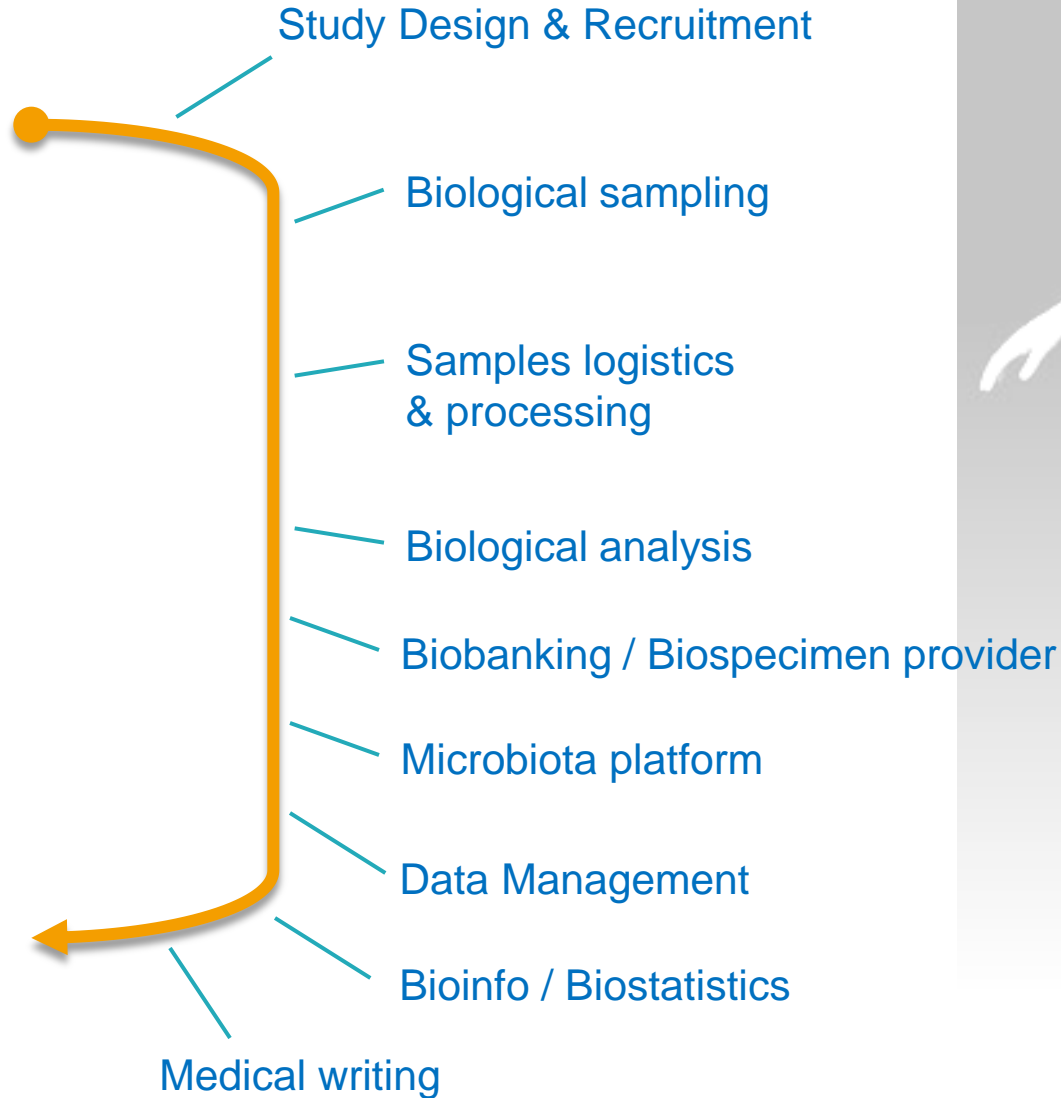
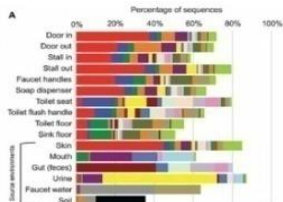
+ according to topics, possibility to integrate other expert managers in Biofortis team
(toxicology, regulatory affairs, ...)



PRESENTATION OF CLINICAL ACTIVITIES



Innovation Services For Industry and Research



Microbiota Monitoring

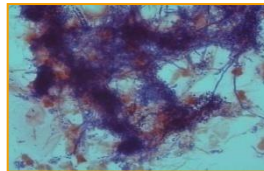


Drugs, Food Supplements, Cosmetics...

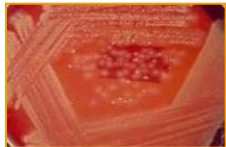
Gut



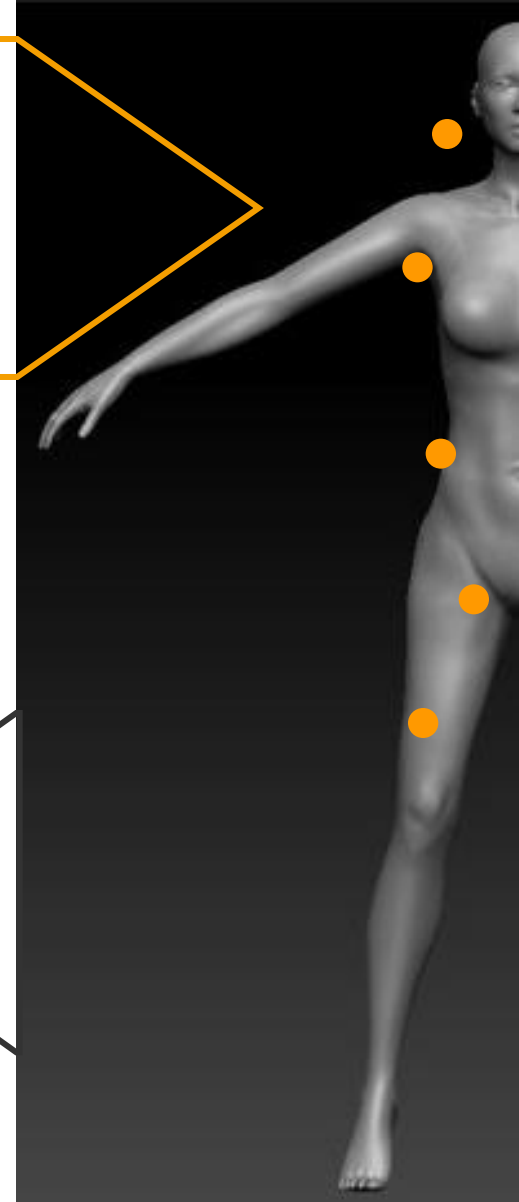
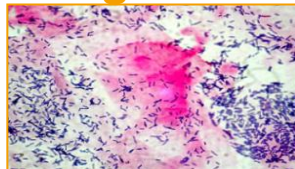
Oral

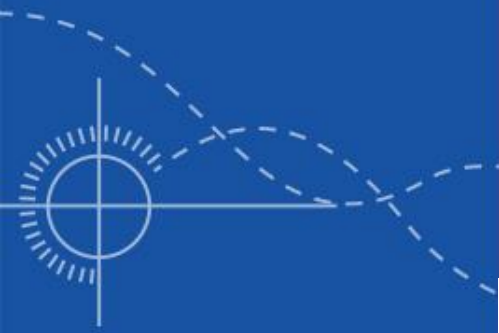


Skin



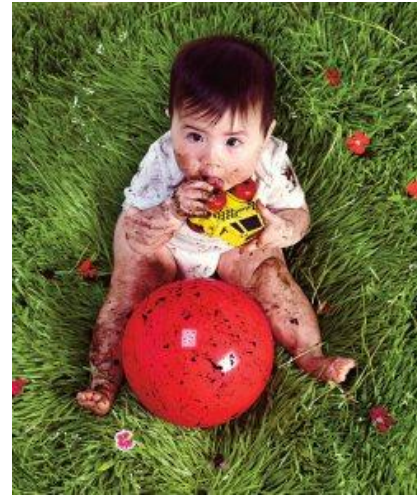
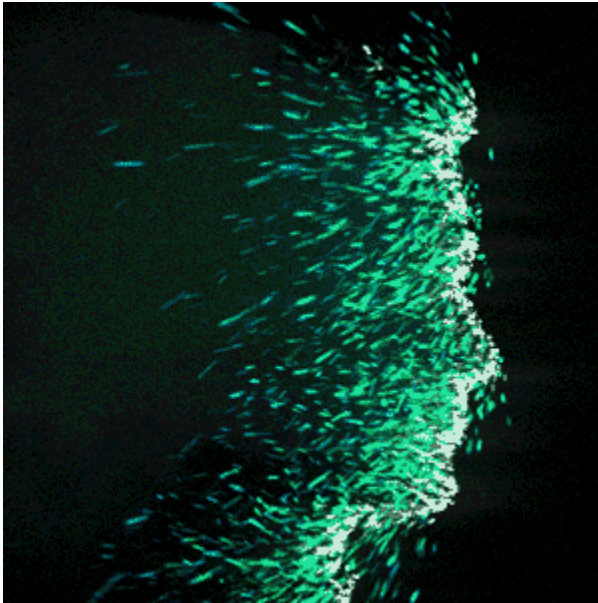
Vaginal





FOCUS ON SKIN MICROBIOTA ANALYSIS



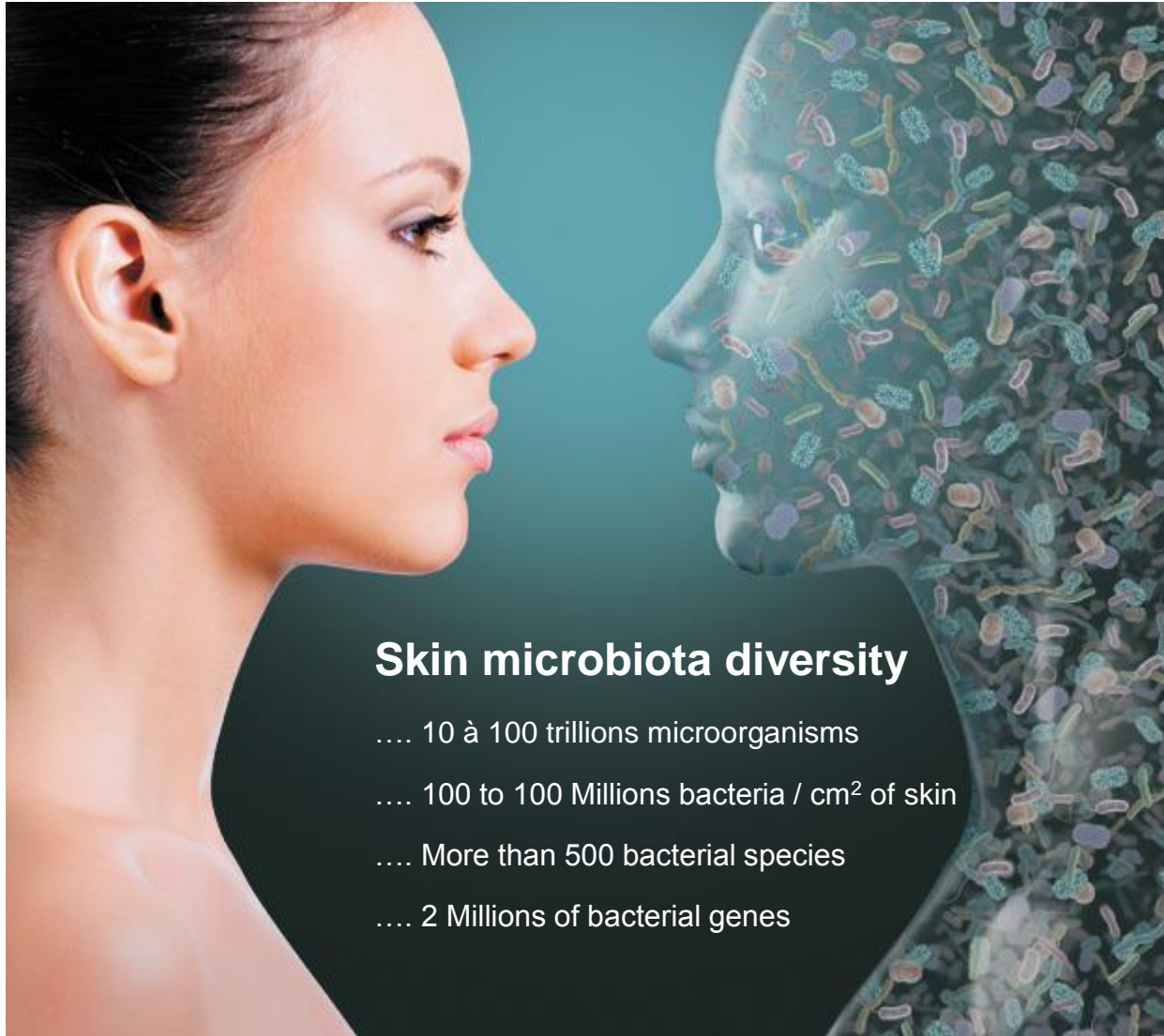


Change of concept : ‘Some of My Best Friends Are Germs’

“We are on the threshold of making profound discoveries about the microorganisms with which we share our bodies”

Mueller et al., 2012 June - Science

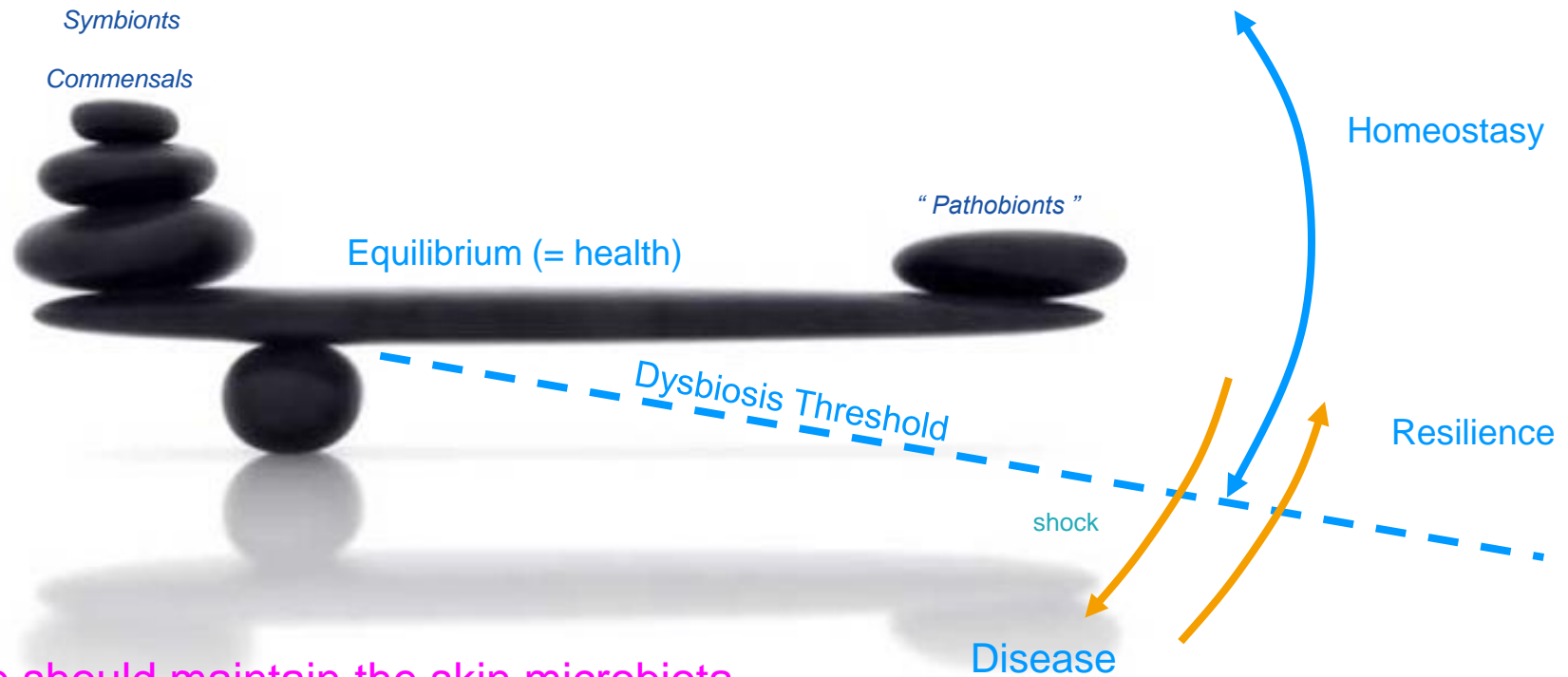




Skin microbiota diversity

- 10 à 100 trillions microorganisms
- 100 to 100 Millions bacteria / cm² of skin
- More than 500 bacterial species
- 2 Millions of bacterial genes

The Human Microbiome : equilibrium



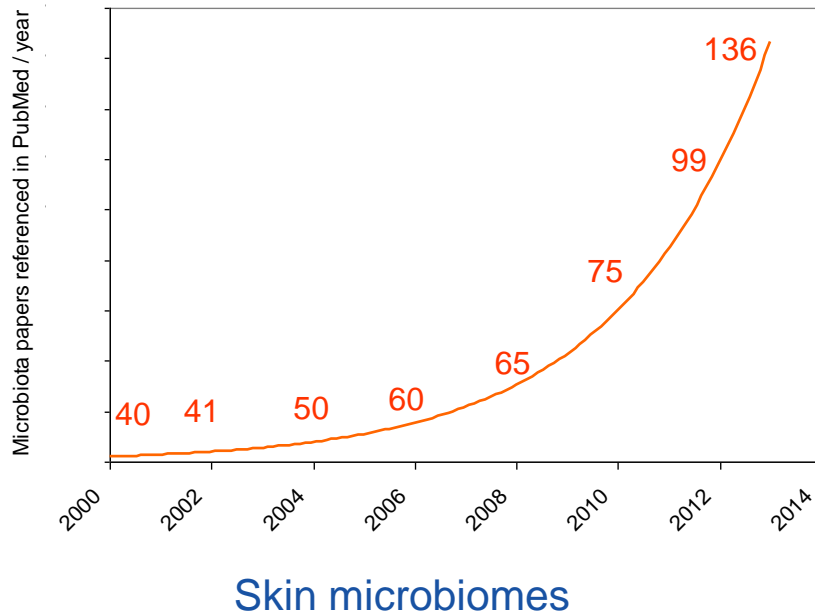
We should maintain the skin microbiota equilibrium to preserve the good physiology of our skin



The Human Microbiome : An Increased Interest



Evolution of the number of publications on skin Microbiomes

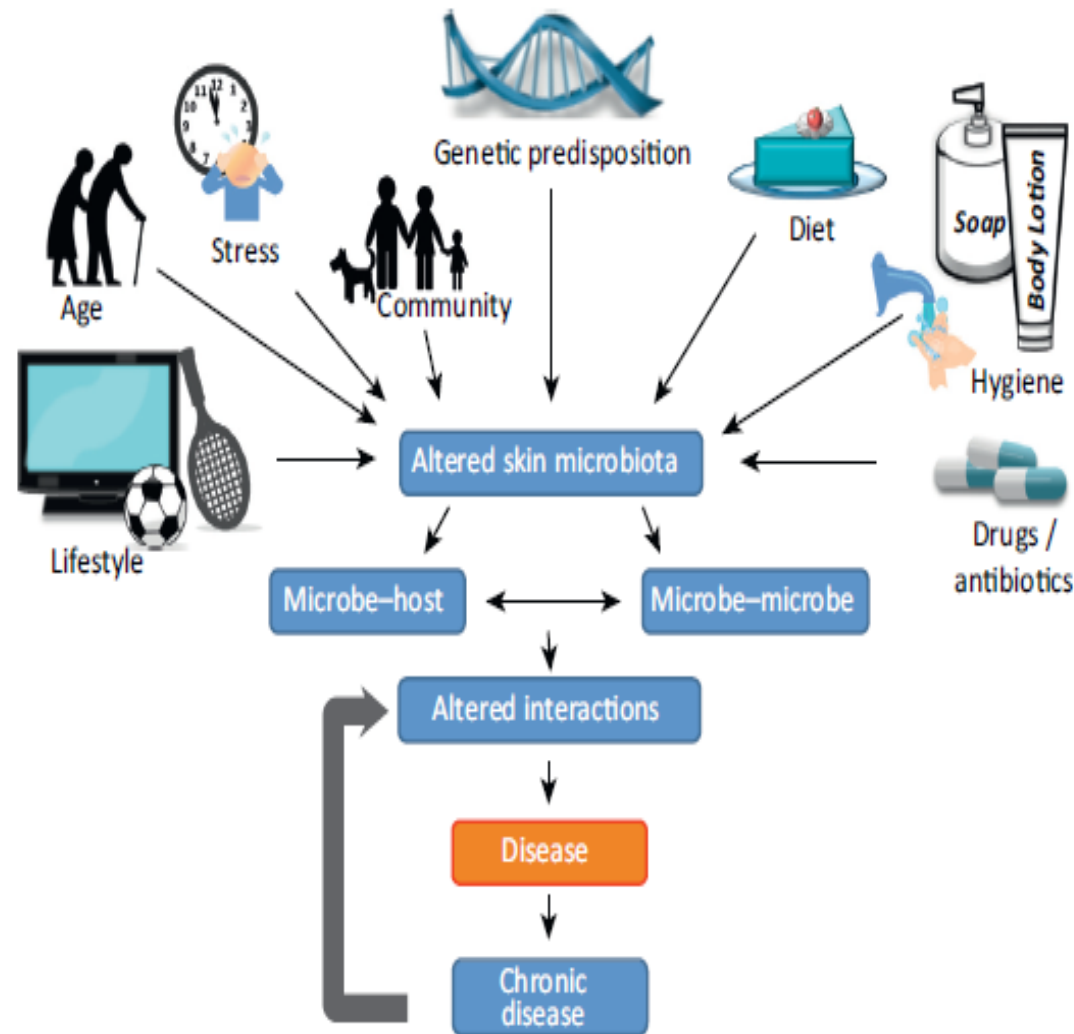


Scientific studies on the Skin flora

- Increase of study report in the last 10 years
- High quality publications (Nature, PNAS, Plos One...)
- Highly health related insight



Factors influencing our microbiome

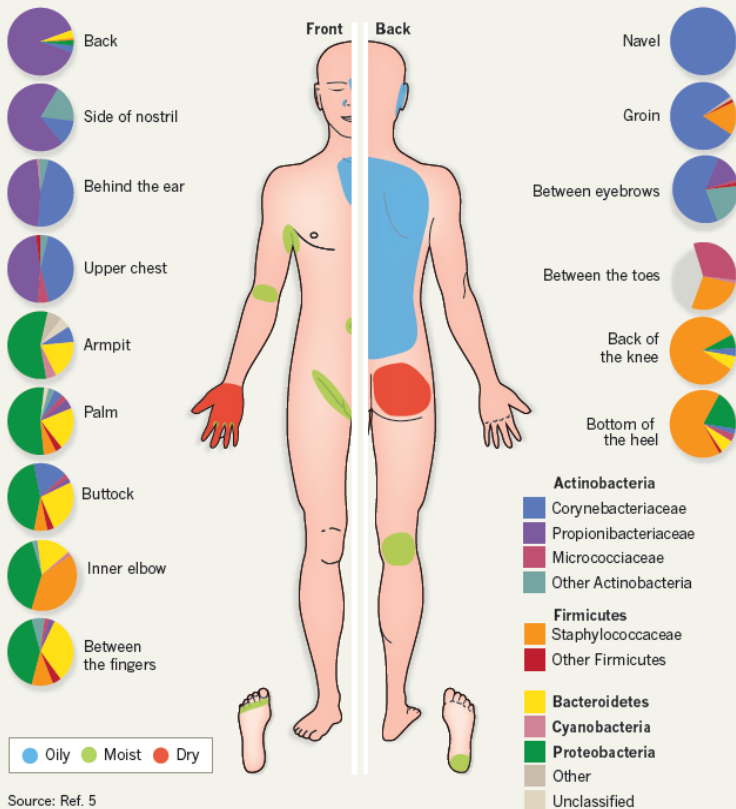


The Human Skin Microbiota - Diversity



MICROBIOME MAP

The human skin is rich with bacteria. The population and ratios vary by region, and depend on the whether the skin site is oily, moist or dry.



Skin Microbiome diversity

- **Four main phyla** : Actinobacteria ; Firmicutes ; Proteobacteria ; Bacteroidetes
- **High diversity according body site**
- **Two hemi-body features are similar** (right & left)
- **Inter-individual variability**
- Differences between **women and men**
- Diversity according **life habit** (personal care, diet, smoking / non smoking, medication...)
- **Quite stable along life adult**

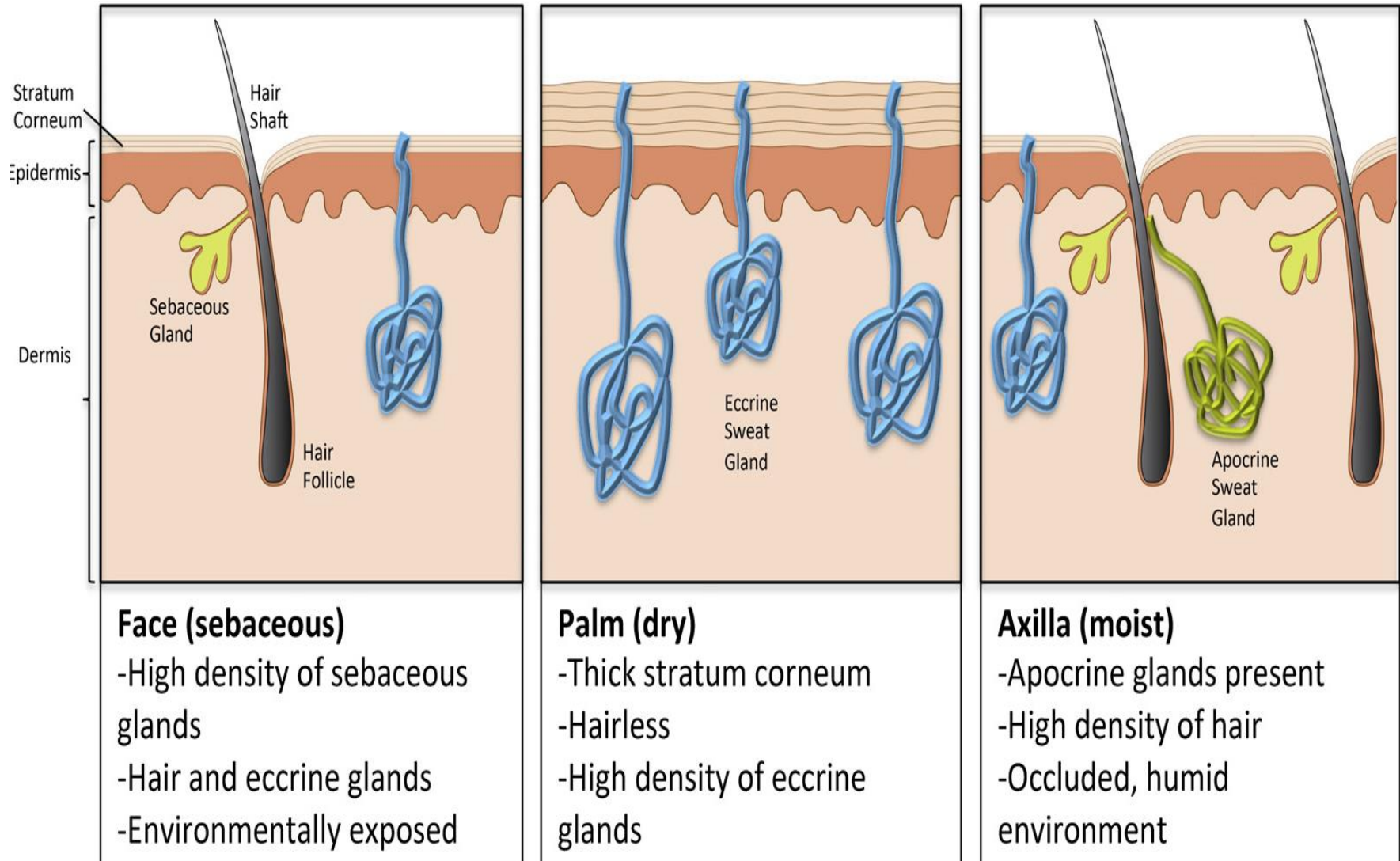
Elisabeth A. Grice, Nature Rev Microb. 2011

Yiyin Erin Chen, J Am Acad Dermatol 2013

The NIH HMP Working group et al Genome Res. 2009



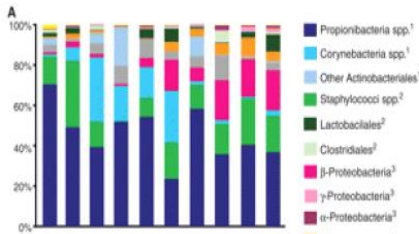
Different environment for the skin flora



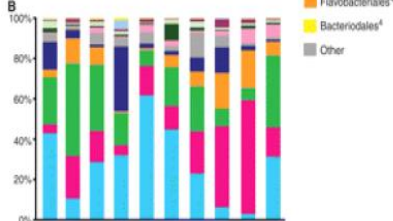
The Human Skin Microbiome - Diversity



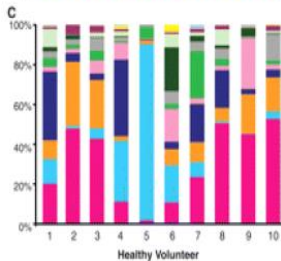
Sebaceous



Moist



Dry



Skin microbiome community

Differences based on skin features

.... Oily skin

.... Moist skin

.... Dry skin

Science 324, 1140 (2009) Elizabeth A. Grice, et al

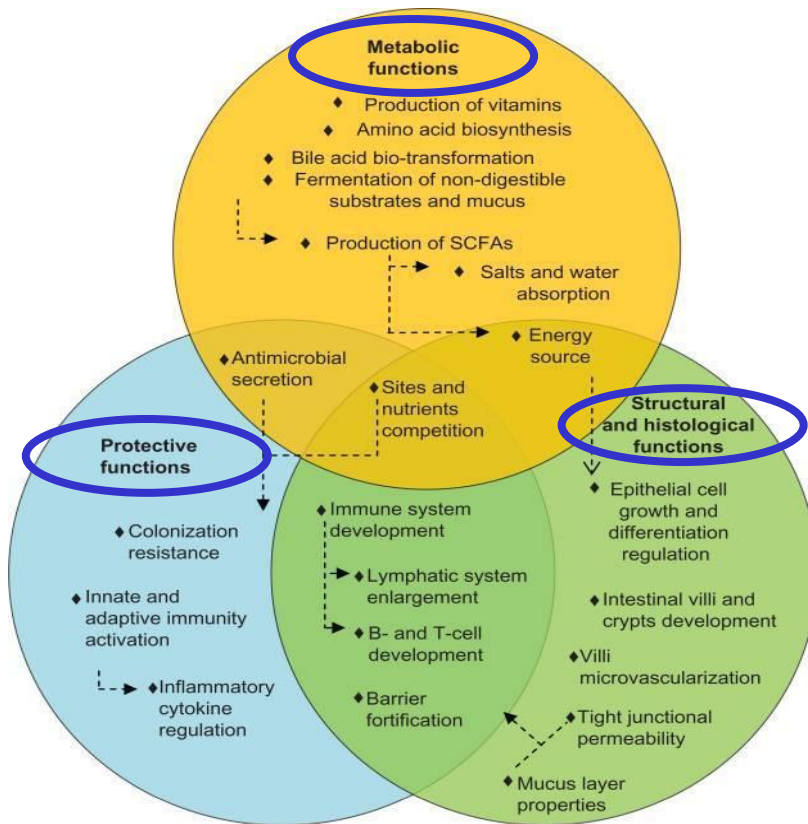
■ *Propionibacteria spp*

■ *Corynebacteria spp*

■ *Staphylococci spp*



The Human Microbiome : A Key Physiological Role In Human Health



Prakash et al., 2011

Gut microbiome : 3 main beneficial functions

- ❑ Metabolic functions
- ❑ Protective functions
- ❑ Structural and histological functions

Link between the gut and skin microbiomes



Immune mediators
in the systemic circulation from
gut to skin and vice versa

Skin Microbiome

- ❑ Protective functions
- ❑ Structural functions



■ **Claims & points of attention**





- **To better characterize the skin microbiome and diversity**

- Health 'indicators' (healthy skin vs pathological skin)

- Inter- and intra- Individual variability (age, stress, geographical origins, body sites, nutritions...)

- **To explore the topical effect of a product on skin microbiota**

- To evaluate non disturbing effect on the skin microbiome

- To identify the benefic effect of a product ('remodeling the Microbiota with skin improvement).

- **To explore the effect of probiotic intake on skin & gut microbiota**

- Correlation of skin & gut microbiota profiles with physiology of the skin (e.g. dry vs moist skin...)

- Effect on skin pathologies = improvement of allergy, reactive skin, dermatite atopic, dandruff...

=> Microbiome equilibrium, richness, diversity.



**New insight for innovation
To developp healthy products**



*“With such knowledge, instead of reaching for a hand sanitizer that kills such populations, we **might soon be able to reach for a product that fertilizes our skin microbiota to improve its ability to resist the colonization by potentially pathogenic organisms.**”*

Schloss *Nature* 2014



“Mother Dirt” Example of fertilization



MEET YOUR SKIN BIOME

The living ecosystem we evolved to keep us healthy.

WELCOME TO THE FIRST
PRODUCTS DEVELOPED FOR
YOUR SKIN MICROBIOME.

Our formulas are based on patented technology and a patent-pending development process. Using biome-friendly products helps rebalance the skin and reduce its dependence on conventional products such as soaps, deodorants, and moisturizers.

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Skin microbiome analysis : points of attention

❑ Skin flora monitoring

.... Need well defined **study design**

.... Need procedure with Quality system for **sampling and storage**

.... Need to define the **molecular methodology for monitoring**

❑ Bioinformatic analysis

.... Need **bioinformatic pipelines** for data analysis

.... Need **microbiota experts** for results interpretation



Clinico-Microbiota Study in Biofortis





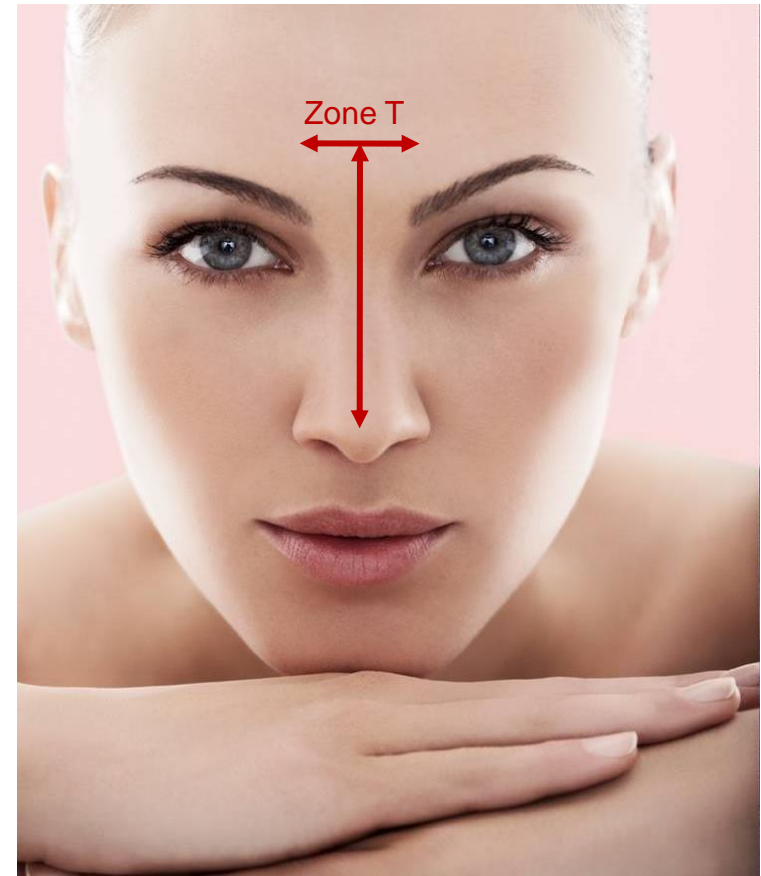
Sampling method

Swabbing method validated

- Non invasive method
- DNA recovery
- Easy to use
- Fast



© PMD Medical

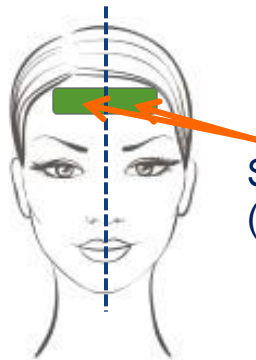


Skin Microbiome Monitoring : Two different approaches / Your claims



Clinical study of microbiota analysis

- Comparative study : each volunteer is his own control
- Product to test versus a control (in hemi-parallele sites)



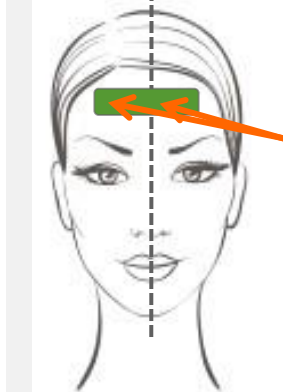
Sampling area
(example)

V0 (screen / inclusion)

Treatment
period

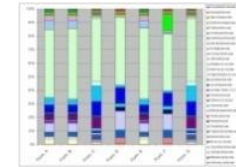


V final



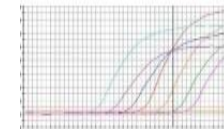
Treated area : 'test
product' (left side) vs
control product (right
side)

Metasequencing approach (Mi Seq Illumina)



- Powerfull approach to determine microbiota composition

qPCR approach



- Micro-organism quantification
- Detection of specific target (genus, species)

Biofortis Microbiota Platform: Metasequencing Analysis



Sample
preparation



Pre-
sequencing



Sequencing



Quality
control

Data analysis

- Taxonomical Metasequencing based on the genes coding for the 16S RNA
- Phylum/Family /genus compositions
- Diversity index / richness

Metasequencing studies help to understand the microbial biodiversity



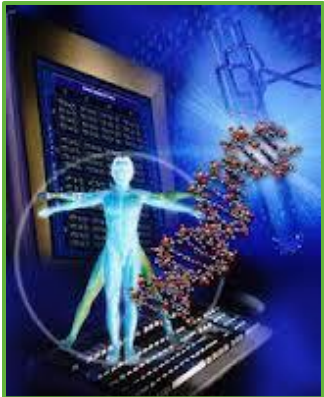
MiSeq Illumina





Data analysis - Level #1 => descriptive statistics will be provided

- OTU (Operational Taxonomic Units) clustering
- Calculation of diversity and richness index
- Taxonomic classification of sequences
- Report including tables and graphs (barplots of taxa relative abundances)



Data analysis - Level #2 => Custom inferential statistical analysis

to be discussed with the Sponsor to define the objectives of the data analysis, which could include:

- Graphical multivariate approaches (ex: hierarchical clustering, PCoA, ...)
- Detection of differentially abundant features between conditions
- Investigation of the relationship between clinical variables and taxa relative abundances
- ...



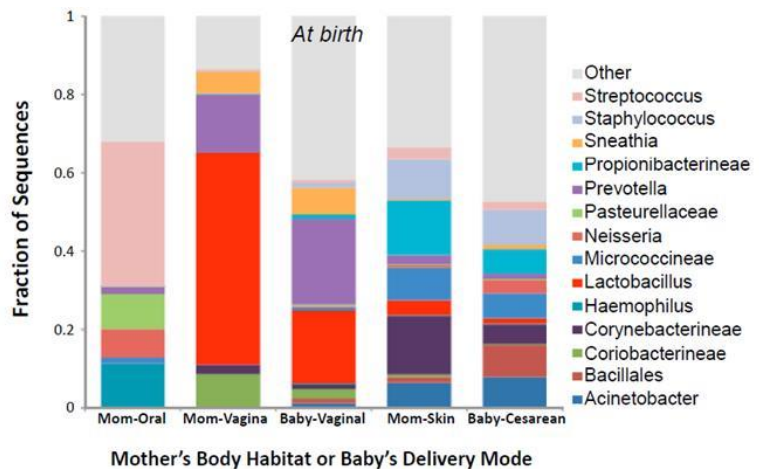
Data analysis of level #3 => Scientific interpretation. Scientific communication.

METASEQUENCING DATA ANALYSIS (LEVEL # 1)

Taxonomical Metasequencing Level # 1: Study of the microbiota composition

- ✓ OTU (Operational Taxonomic Units) clustering
 - ✓ Taxonomic classification of OTUs
 - ✓ Calculation of diversity and richness index
 - ✓ Report including tables and graphs (barplots of taxa relative abundances)
- Only descriptive statistics will be provided

Example : Microbiota composition (Genus)



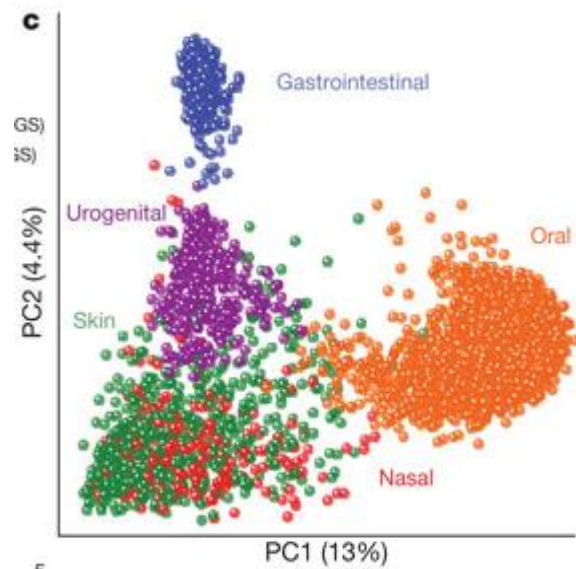
Dominguez-Bello, et al. *Proc Natl Acad Sci.* 2010;107:11971-11975.



Taxonomical Metasequencing Level # 2: Study of the microbiota composition

Custom inferential statistical analysis, to be discussed with the Sponsor to define the objectives of the data analysis, which could include:

- ✓ Graphical multivariate approaches (ex: hierarchical clustering, PCoA, ...)
- ✓ Detection of differentially abundant features between conditions
- ✓ Investigation of the relationship between clinical variables and taxa relative abundances
- ✓ ...



*PCoA: Principal coordinates analysis (or classical multidimensional scaling), a statistical method used to explore similarities in data set.
Source HMP*



Taxonomical Metasequencing Level # 3: Study of the microbiota composition

- ✓ Scientific interpretation with reviewing the litterature
- ✓ Link with other biological parameters (clinical data)
- ✓ Next strategy proposal
- ✓ Scientific communication (poster, publication...)

Adhoc solution / support from A to Z





Krona zoomable pie charts (Ondov et al., 2011)



C:\Users\
no\Desktop\examf



Make your product respectful of skin health

- The **skin microbiome** strongly contributes to **healthy skin**
 - **Skin barrier** integrity and **homeostasis**
 - Role against **pathogens**
 - Enhancement of the **immune system**
- Biofortis can assist you all along your product life cycle to:
 - Investigate the **efficacy and safety** of your product on skin health (preservation, modulation...)
 - Improve the effect of your product on
 - **Screen the right formula** (ingredient, active compound, optimal dose...) to prevent skin disorders or to preserve the skin flora equilibrium and diversity
 - **Develop specific products** for a proper skin care according to skin diversity (ethnicities, life habits, environment...)



Thank you for your attention !

