

# Dermocosmetic strategies to rebalance the skin's ecosystem

San Diego, October 29-30 , 2018

 **BASF**  
We create chemistry

Care  
Creations™

# BASF – We create chemistry

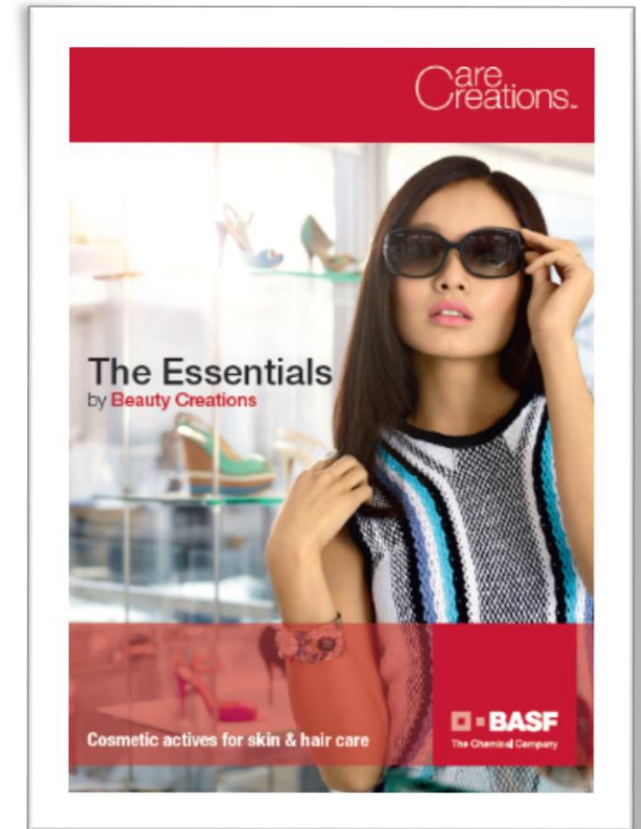
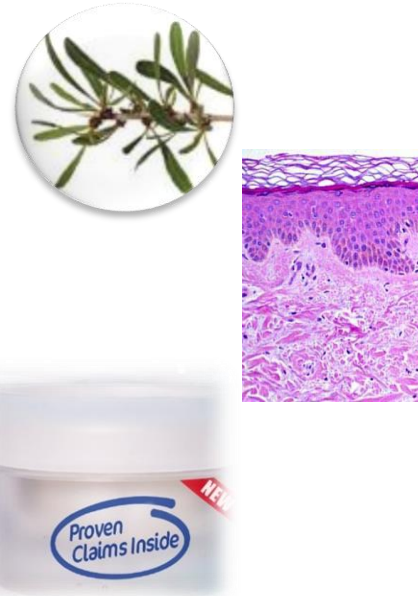
- Our chemistry is used in almost all industries
- We combine economic success, social responsibility and environmental protection
- Sales 2017: €64,475 million
- EBIT 2017: €8,522 million
- Employees (as of December 31, 2017): 115,490
- 6 Verbund sites and 347 other production sites



# BASF Bioactives business Overview

Beauty Creations is the cosmetic active ingredients business of BASF Personal Care and is the leader in its field

- Products are mostly plant extracts with focus on origin and sustainability
- Supported by a biological mechanism of action
- With scientifically, clinically proven performance



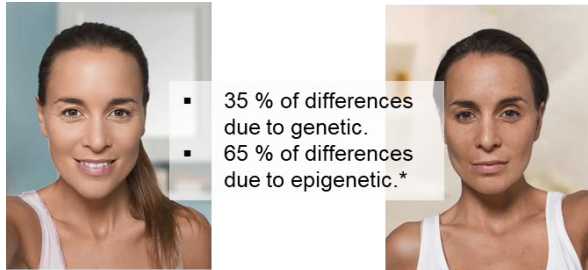
Bioactives are at the heart of the Personal Care market

# BASF Bioactives business Overview

## Epigenetics

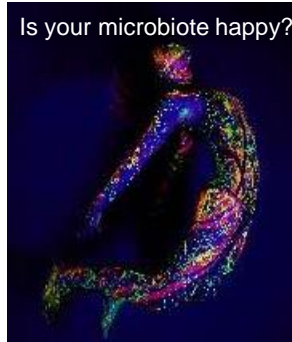
Epigenetics refers to mechanisms regulating gene code reading that highly contributes to aging and environmental induced changes. Epigenetic management could help restore sleeping beauty.

Epigenetics is for instance what makes twins look different



The older you are, the more epigenetic marks you have in your genes.

\* Graham. Twins exhibit differences in gene expression. Scientific American. 2005



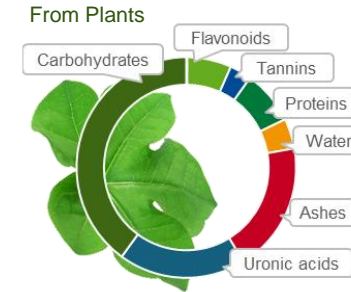
## Microbiota

100 billion microorganisms use our skin as their habitat and are the guardians against potentially harmful invaders. But the balance is fragile.

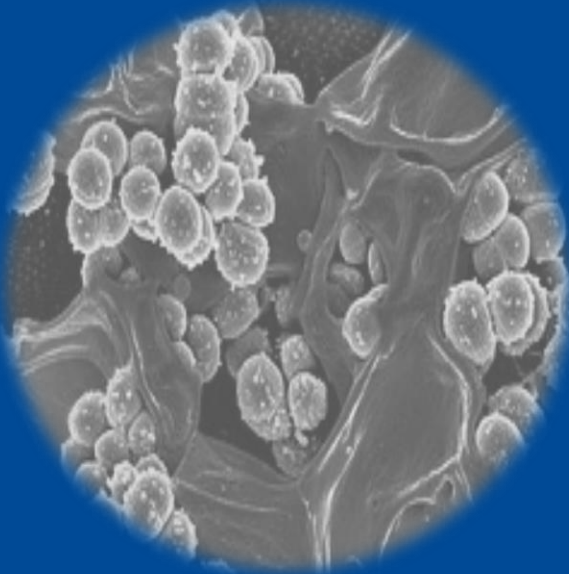
To push back the boundaries of skin care products, we have to look at every single element that participate to skin health and beauty.

## Extraction & process differentiation

Increasing regulatory constraints reduce the open space for product innovation. Developing unique, socio- and eco-responsible extraction methods or processes is key to keep bringing innovative ingredients on the market.



We focus on 3 strategic innovation platforms to differentiate

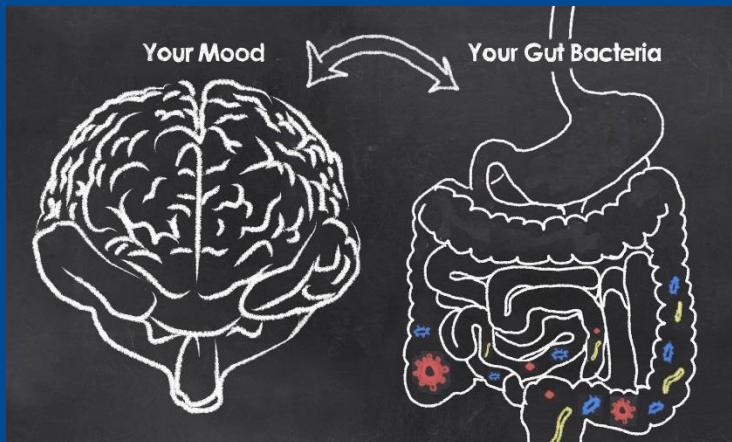
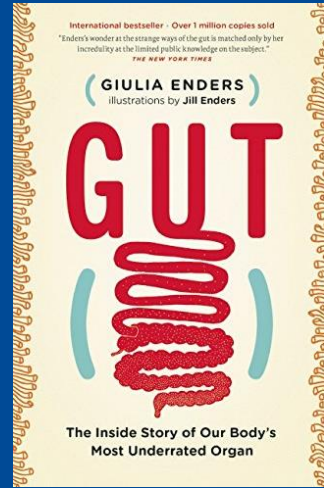


## AGENDA

- Microbiome and market opportunities in Personal Care
- How do we address those opportunities?
- Our recent achievements

# Microbiota **revolution**

From profound  
intimacy...



Medicine



Cosmetic

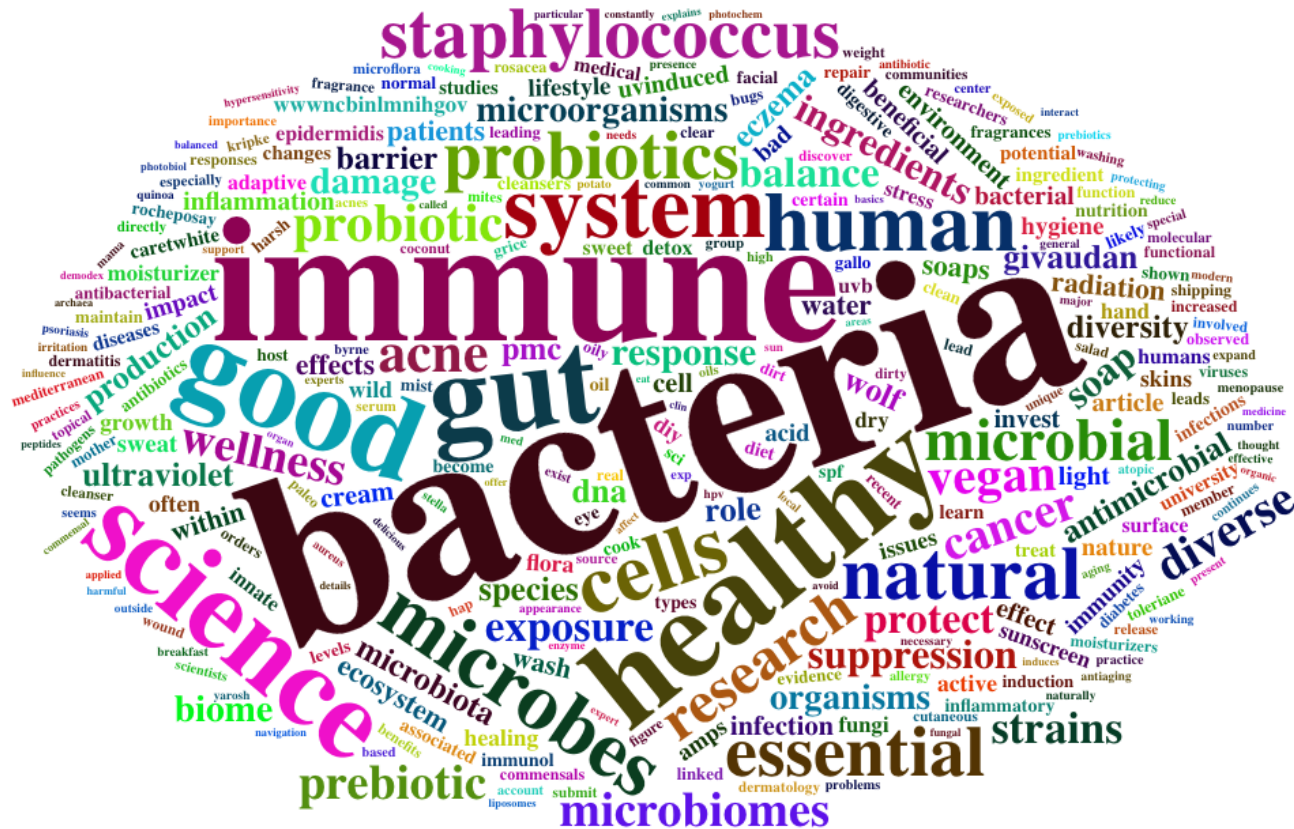


Food and  
nutrition



...to the market place

# Microbiome trend in Personal Care Industry



Word cloud created based on BASF big data analysis

A science-based skin care trend

Fits healthy trend



Protection and prevention

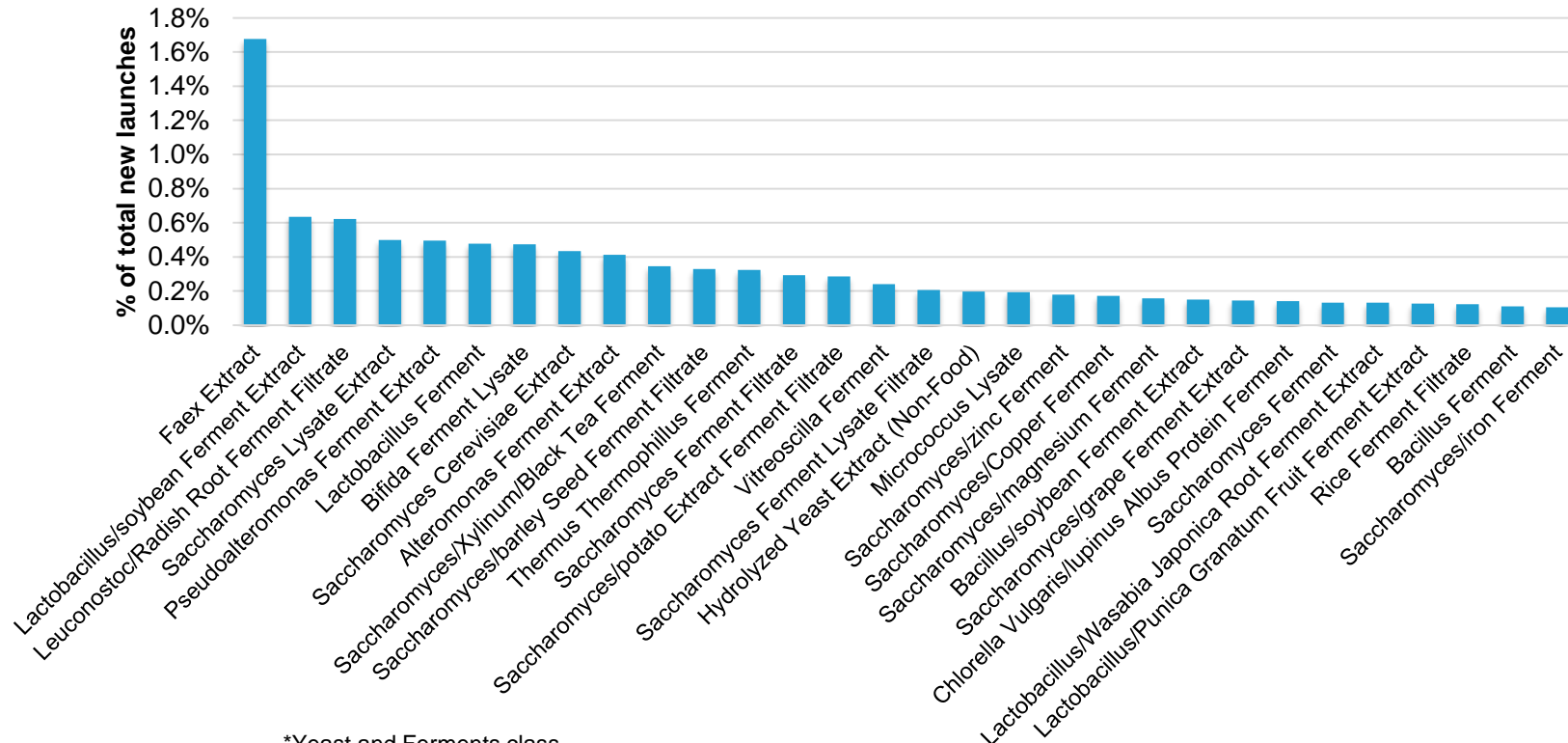
Fits both natural and dermocosmetic brand



# Microbiome: Probiotic fermented ingredients

Majority of “ingredients” are ferments, ferment lysates or ferment lysate filtrates generated from incubation of a microorganism (such as a probiotic) in culture with a food source

Global launches of Skin Care products with microorganisms\* – Top 30



\*Yeast and Ferments class

Formulated with  
50% probiotic extracts



The major described claims address sensitive & aging skin and skin perfection (oily skin) or scalp.

Few skin microbiote analysis before/after application.



# The microbiota lives with us and suffers with us!

## Behavioral factors

### Stressful life

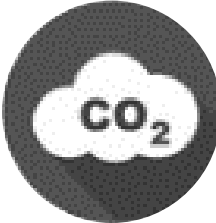
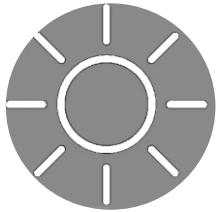


### The cult of hygiene...



## External factors

### Environmental factors

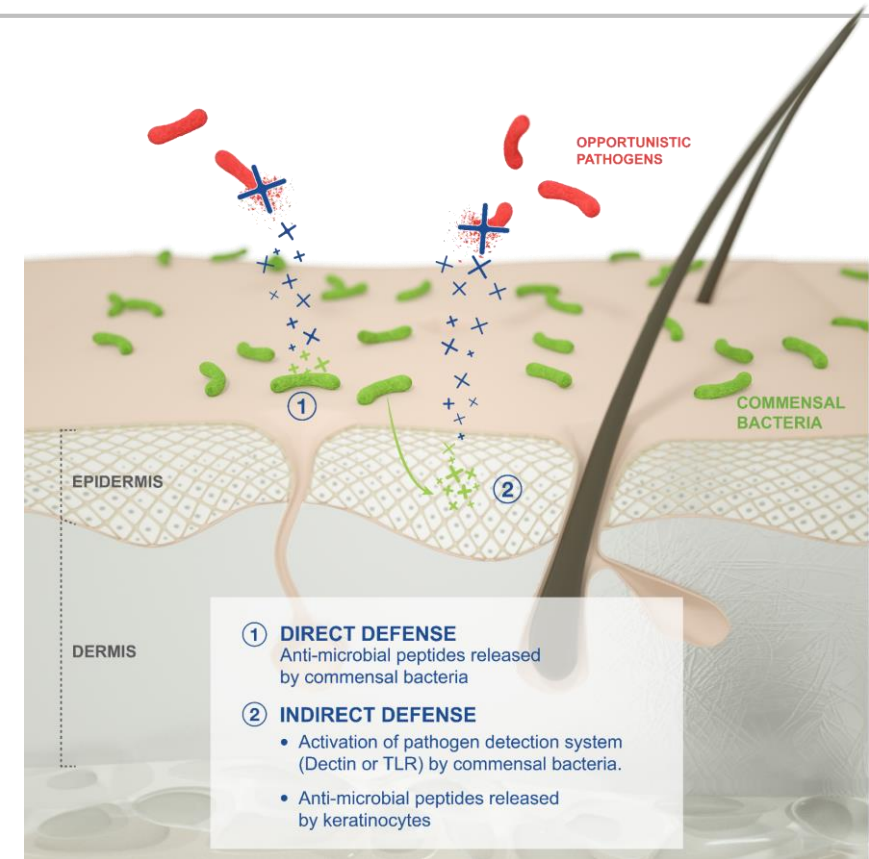


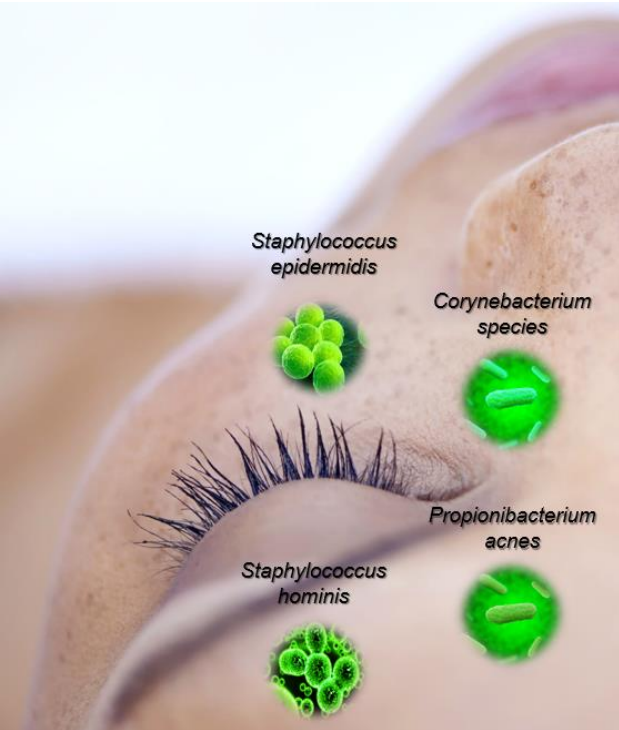
# Skin microbiome - A fragile balance

Commensal bacteria live in community and in harmony with skin cells. This ecosystem is a fragile balance.

Skin cells bring nutrients and are the foundation on which commensal bacteria can multiply. In exchange, a healthy commensal flora actively prevents from the colonization of the skin by opportunistic pathogens.

By secreting anti-microbial peptides (direct defense) and stimulating the natural defenses of skin host cells (indirect defense), commensal flora forms a double line of defense against opportunistic pathogens.





## COMMENSAL BACTERIA

Resident flora that lives in harmony with skin cell

- *Staphylococcus epidermidis*
- *Staphylococcus hominis*
- *Corynebacterium species*
- *Propionibacterium acnes*

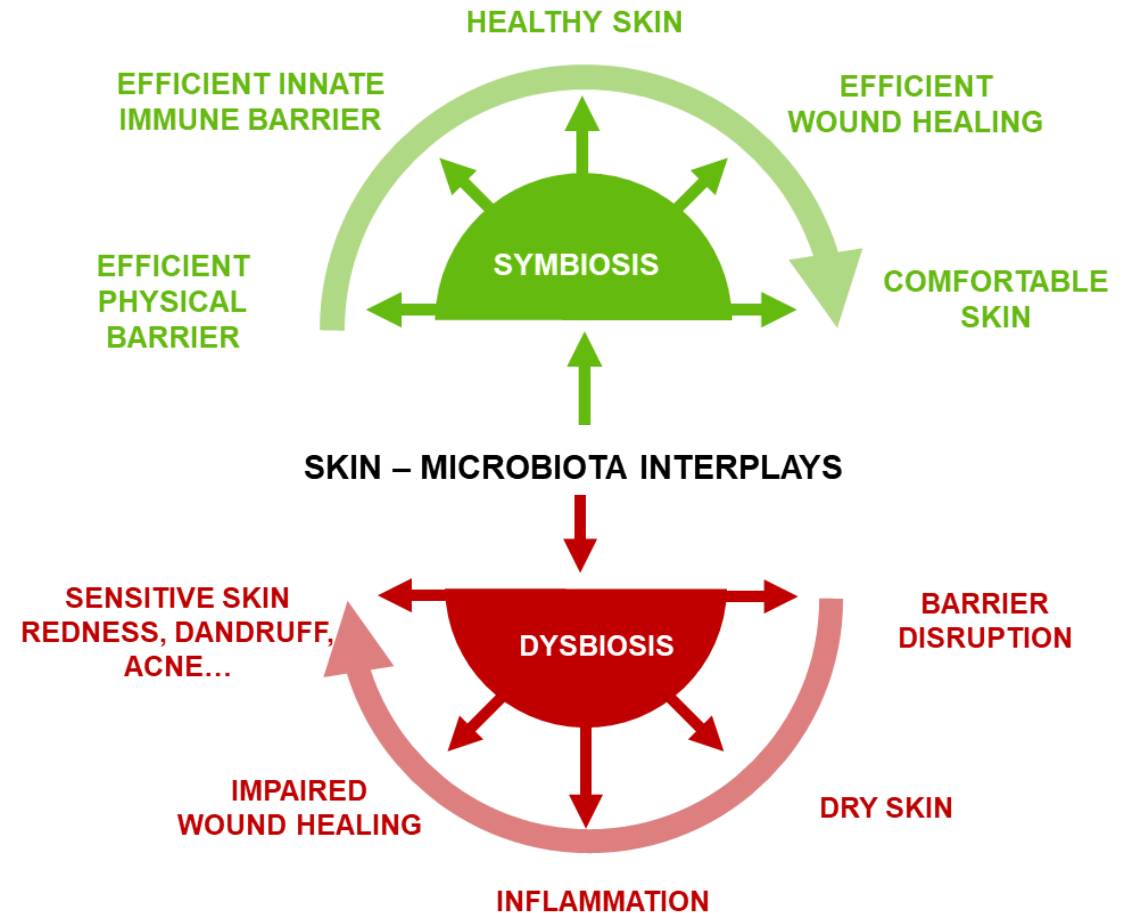
## OPPORTUNISTIC PATHOGENS

Present on skin surface, but replace commensal bacteria and evade the immune system and cause inflammation

- *Staphylococcus aureus*
- *Pseudomonas aeruginosa*
- *Propionibacterium acnes*



## Symbiosis & Dysbiosis



# Imbalance of microbiota in skin conditions

## Ultraviolet radiation (UVA and UVB)



The sensitivity of various microbes to UVR as well as their re-colonization potential following exposure differed  
P582 SID 2015 - P591 SID 2017

## Sensitive skin and inflammation



*Bacillus cereus* increases  
PLoS One 2013 Nov 8;8(11): e78773

## Scalp Dandruff



Association of *Malassezia* species with dandruff  
Indian J Med Res. 2014 139(3): 431-437.

## Dry Skin / Atopic dermatitis



Increased microbial burden particularly *S. aureus*

Analytical Cellular Pathology  
Volume 2018, Article ID 1956403,

Dermal adipocytes protect against *S. aureus* skin infection thanks to cathelicidin secretion from differentiating adipocytes

Science. 2015 Jan 2; 347(6217): 67-71.

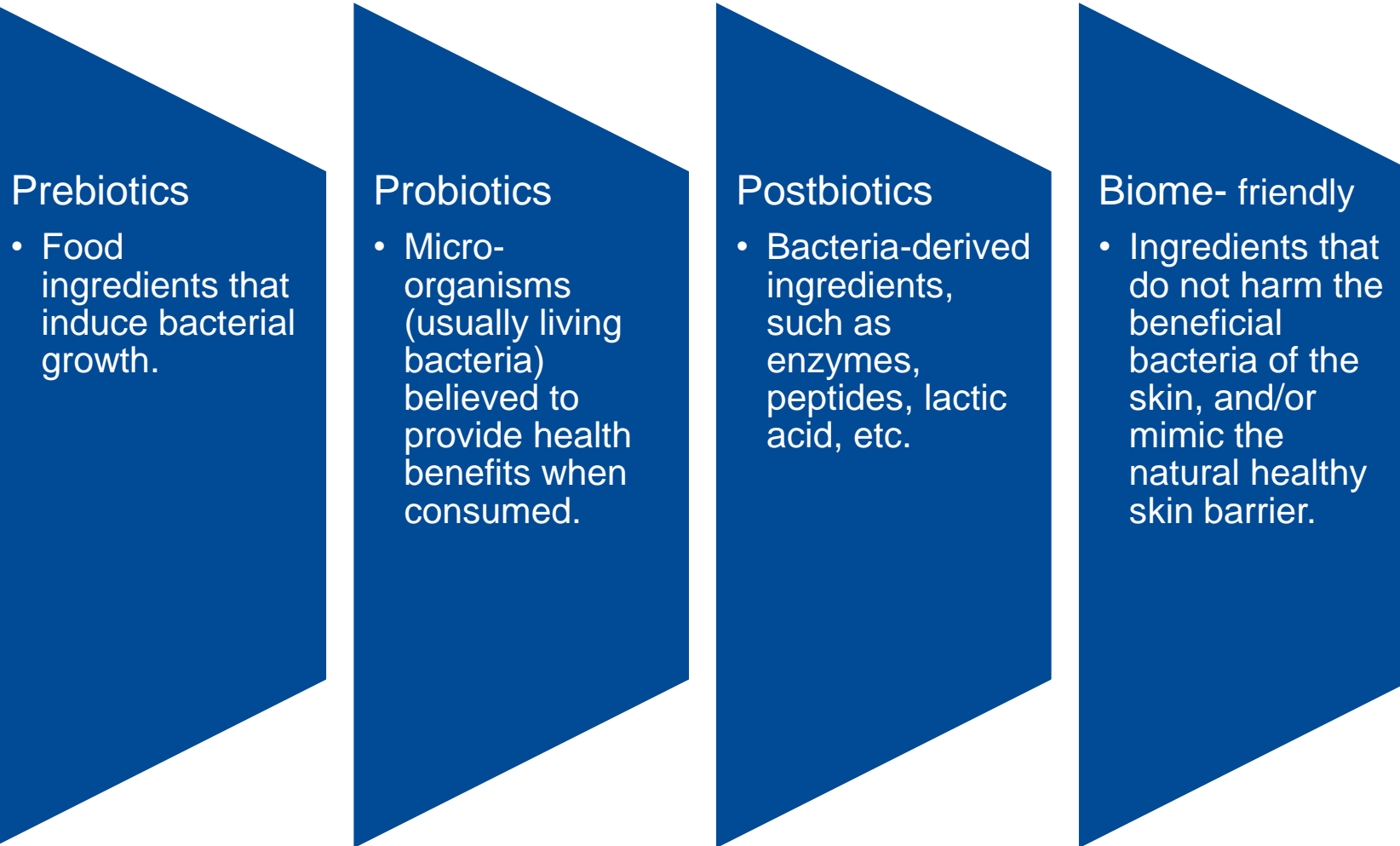
## Acne

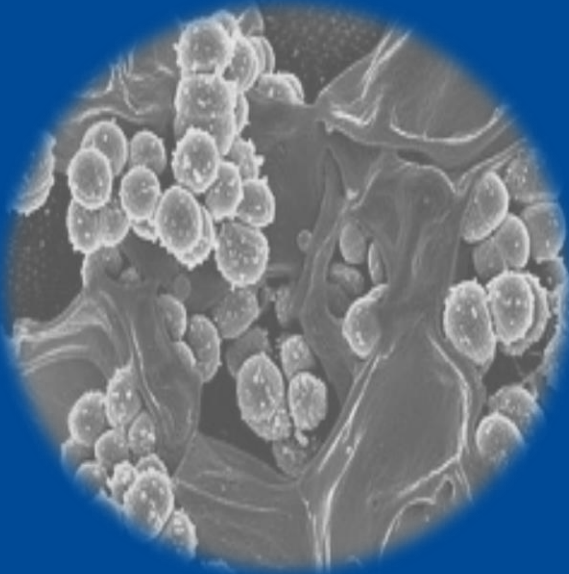


*Propionibacterium acnes* (now *Cutibacterium*) implicated in acne inflammation and pathogenesis

JEADV 2018 32(2):5-14.

## Four main ways to enhance skin care to address the microbiome





## AGENDA

- Microbiome and market opportunities in Personal Care
- How do we address those opportunities?
- Our recent achievements

## BCS Microbiota platform created in April 2016

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As the recent advances in genomics have made it possible to reveal the complexity of skin microbiote composition, we are only now beginning to foresee the beneficial role of this cutaneous microbiota and to establish a link with the health of our skin.



Through a platform dedicated to the study of this cutaneous microbiota, BASF is continually acquiring a deeper understanding of the interactions between the skin and its microflora to offer unique active ingredients able to rebalance cutaneous microbiota.

**For an out of the box cosmetic, which regulates the cutaneous disorders by acting on the living.**

# BASF Performance Biologicals

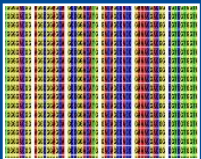
## BASF Bioscience Research Competencies



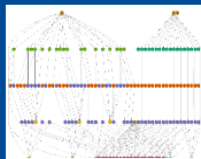
Microbiology & Molecular Biology



Next Gen DNA Sequencing



Bioinformatics



Genetics



Biology



Phenotyping

## Performance Biologicals

Leverage internal and external expertise

Deliver on consumer demands

Leapfrog to next generation products

## Customer Demand



Agriculture



Personal Care



Nutrition

## Product area

■ Disease control

■ Insect control

■ Skin Care

■ Scalp Care

■ Human Nutrition

■ Animal Nutrition

**New Products**  
**+**  
**New Claims**



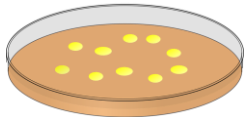
# Our organization

## A team with multidisciplinary competencies:

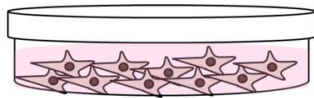
More than 25 experts (Market analysis, R&D, Data Mining) dedicated to:

- Increase our knowledge on skin microbiote and related skin care market
- Develop multifaceted models to study the impact of ingredients:
  - On microbiota, and skin cells and environmental aggressors such as UV, pollution particles, etc.
  - In the context of multiple categories of microorganisms

Bacterial cells



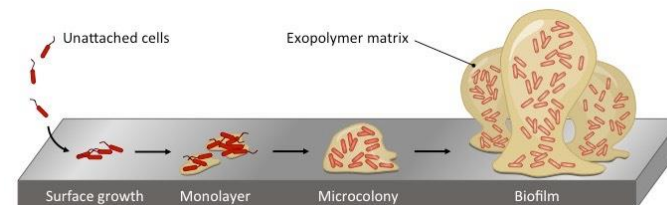
Skin cells



Environmental factors



Biofilm formation



Clinical studies+ genomics

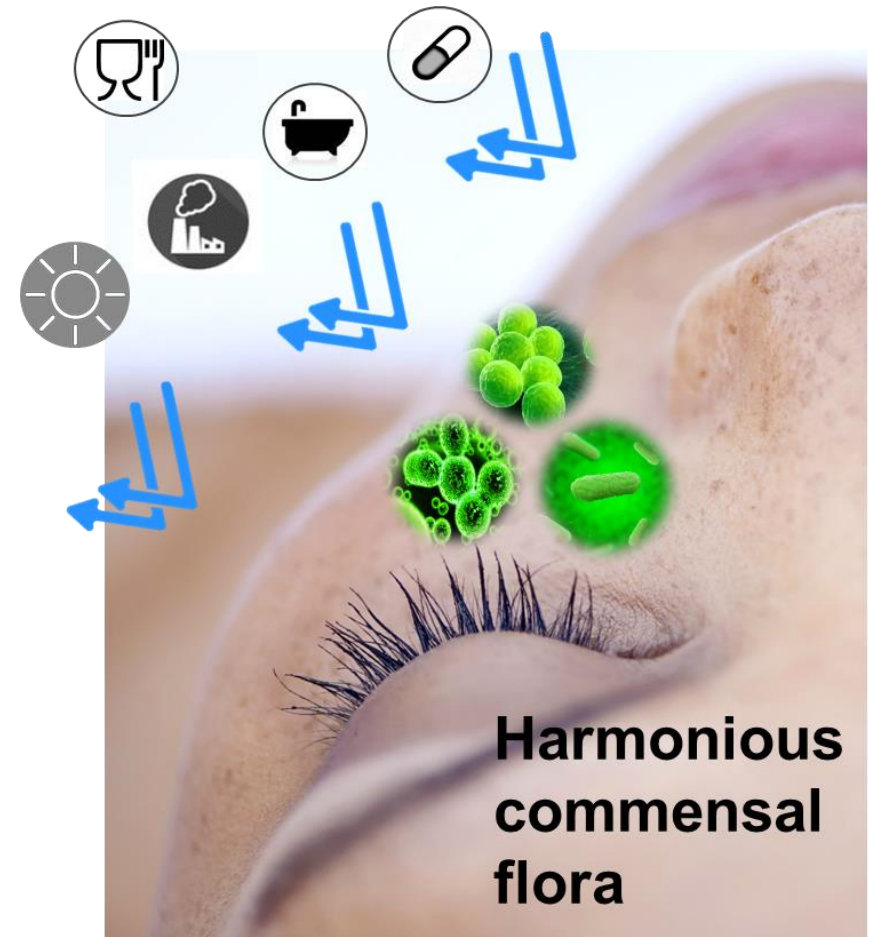


# Our aim: To promote a healthy ecosystem

**Dysbiosis** is due to a change in the composition of the commensal bacterial ecosystem (increase or a decrease in the bacterial diversity of commensal flora).

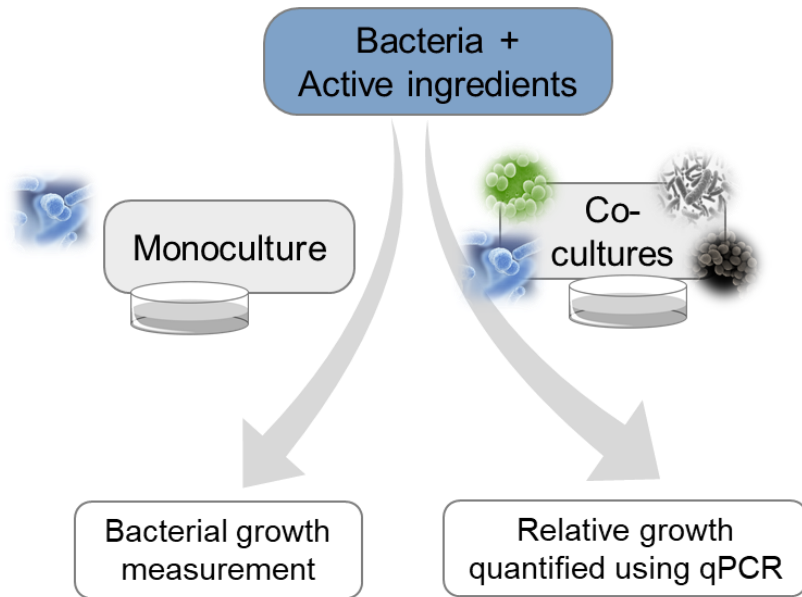
As a consequence, opportunistic pathogens colonize the skin. Dysbiosis may lead to inflammation and/or skin disorders.

**Regulating the ecosystem** not only means favoring commensal bacteria over pathogens, but also protecting the bacteria against environmental factors and controlling the behavior of the bacterial population (virulence factors).

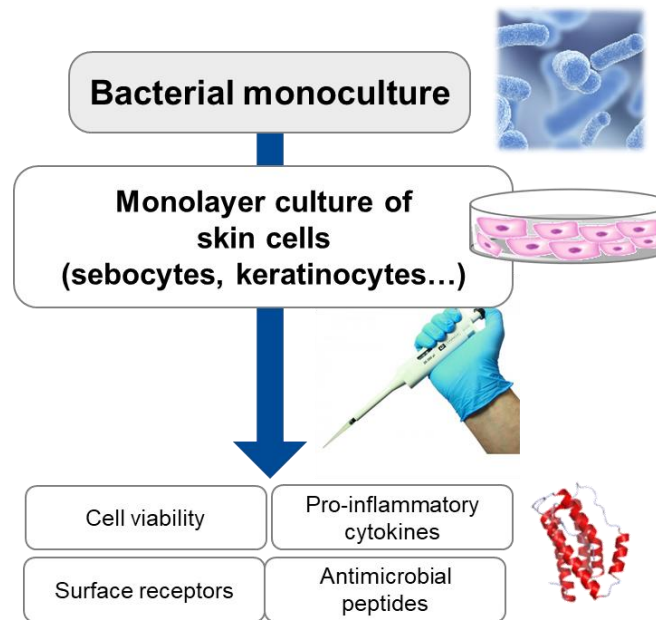


# Models to study microbiota and skin interactions

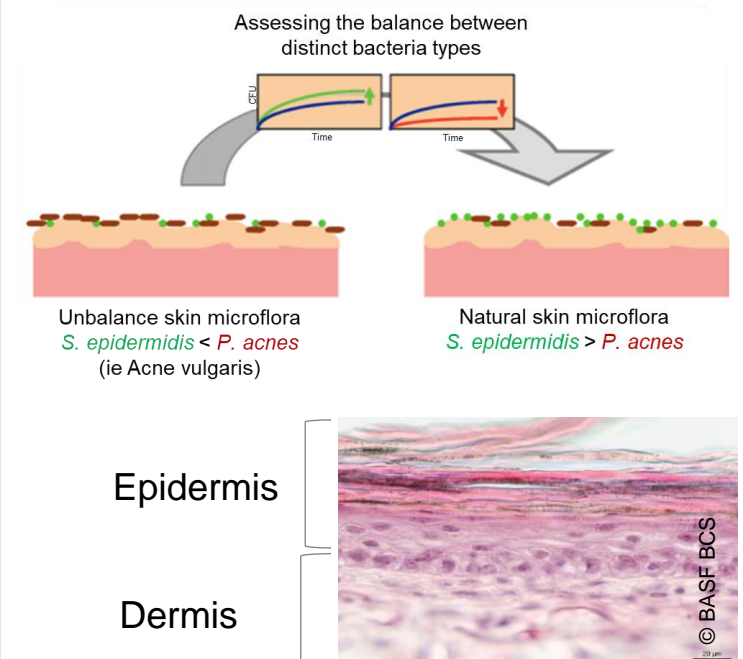
## Active ingredient and single or mixed microbial cultures



## Single layered Skin cells and single microbial co-cultures



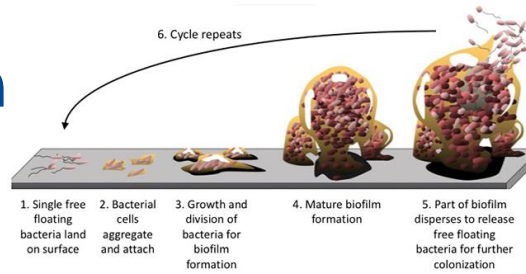
## Different types Skin cells and mixed microbes model



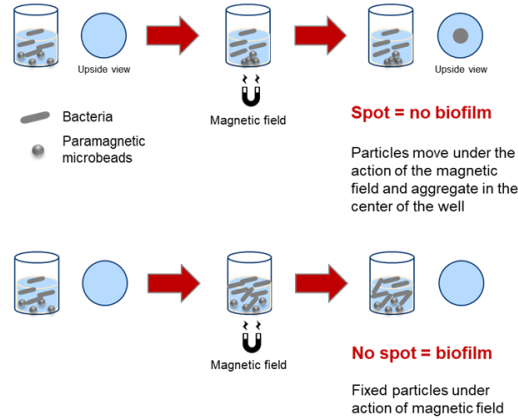
**Need for complex models to study effect of ingredients on microbiota and its ecosystem**

# Advanced systems to study microbiota

## Virulence evaluation

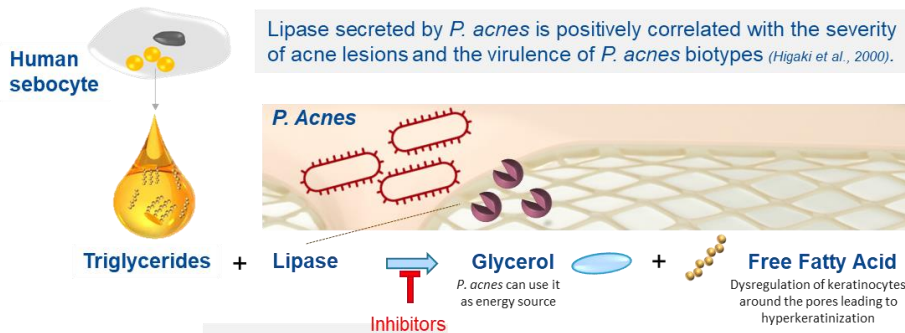


Biofilm formation is a main virulence determinant in infection by *Staphylococcus aureus* isolates (McCarthy H. et al., 2015).



## Biofilm formation

## Virulence factor



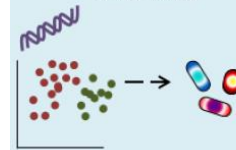
## Studies on human panelists



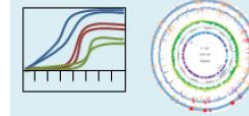
### DNA-Based Approaches

Who is there?  
What can they do?

16S rRNA, 18S, ITS gene sequencing



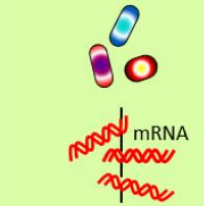
metagenomics



### RNA-Based Approaches

How do they respond?  
What pathways are activated?

metatranscriptomics

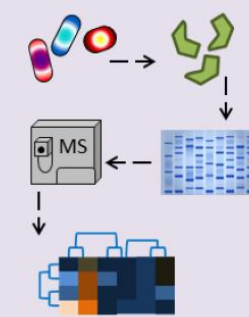


enzymes

### Protein-Based Approaches

How are they interacting with the host?  
What proteins are being produced?

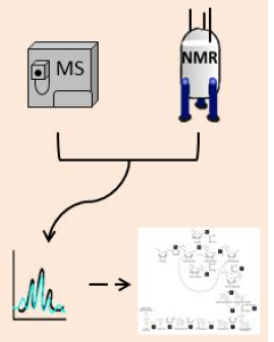
metaproteomics



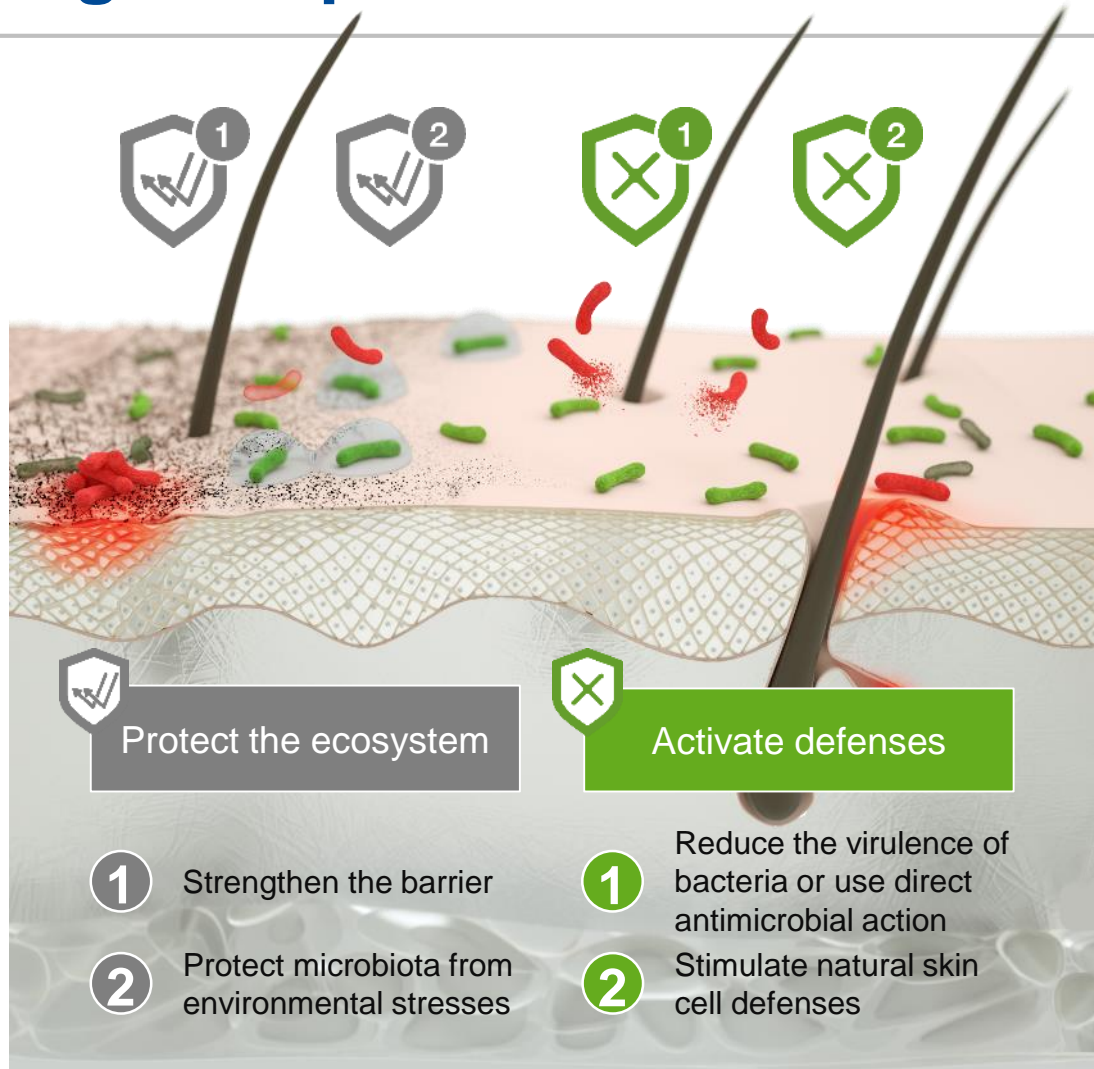
### Metabolite-Based Approaches

What are the chemical outcomes of their activity?

metabolomics



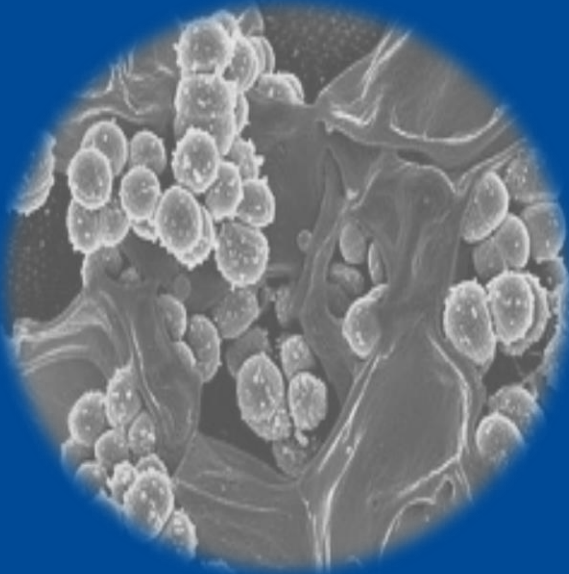
# Our strategy: Enabling the optimization of the cutaneous microbiota



BASF develops ingredients **enabling the optimization of the cutaneous microbiota**.

The first strategy is a **dual protective approach** to promote a harmonious development of the ecosystem  
Our ingredients **strengthen the barrier and/or protect the commensal flora** from the main environmental factors that may have a deleterious effect on bacteria.

The second strategy is to actively **promote innate defenses against opportunistic pathogens** at both microbiota and skin cells levels.



## AGENDA

- Microbiome and market opportunities in Personal Care
- How do we address those opportunities?
- Our recent achievements



|                                      | Betapur®  | Bix'Activ®  | Relipidium®                                    | Phytosoothe®  | PatchH <sub>2</sub> O®                              | Purisoft®                               |
|--------------------------------------|---|---|--|---|---|---|
| <b>Ecosystem</b>                     |   |   |  |   |   |   |
| Strengthens the barrier              |   | ●   | ●  | ●   | ●   |   |
| Protects microbiota                  |   |   | ●  | ●   | ●   | ●                                       |
| <b>Defenses</b>                      |   |   |  |   |   |   |
| Anti-microbial / virulence action    | ●   | ●   |  |   |   |   |
| Stimulates natural skin cell defense | ●   |   | ●  |   |   |   |
|                                      | ▼   | ▼   | ▼  | ▼   | ▼   | ▼                                       |
|                                      | <i>Double line of defense against impure skin</i> | <i>Dual "protector and defender" ally against skin imperfection</i> | <i>Healthy ecosystem defender for dry skin</i> | <i>Double line of protection for fragile and sensitive skin</i> | <i>Comprehensive optimizer of urban skin health</i> | <i>Microbiota anti-pollution shield</i> |

# Purisoft<sup>®</sup>, PatchH2O<sup>®</sup> and Bix'Activ<sup>®</sup> - *in vitro* results



**Purisoft<sup>®</sup>**  
Moringa Oleifera Seed Extract

**PatchH2O<sup>®</sup>**  
Hydra-protect Technology

**Bix'Activ<sup>®</sup>**  
Bixa Orellana Seed Extract

## Microflora protection

2 x

Protects commensal bacteria against PM 2.5 (*S. epidermidis*)

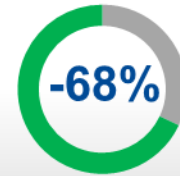
1.5 x

Protects commensal bacteria against PM 2.5 (*S. hominis*)

## Microbiota optimization



Preservation of beneficial skin microbiota against pollution (*S. epidermidis* / PM 2.5)



Reduction of opportunistic bacterial virulence (biofilm formation by *S. aureus*)

## Microbiota virulence



*P. acnes* virulence (lipase) without direct effect on bacteria growth

Dry & urban skin

Acneic skin



# Betapur<sup>®</sup>, Relipidium<sup>®</sup> and Phytosoothe<sup>®</sup> - results



## Betapur<sup>®</sup>

*Peumus Boldus* Leaf Extract

## Relipidium<sup>®</sup>

Yeast extract biofermented by *Lactobacillus plantarum*

## Phytosoothe<sup>®</sup>

*Brassica Campestris* (Rapeseed) Sterols and Cetearyl Alcohol

### Microbiota optimizer

*In vitro*



Decrease in *P. acnes* growth and in *S. aureus* growth (at 1%, indicator of the severity of acne)



Stimulation of the skin's natural antibacterial system ( $\beta$ -defensin hBD-3)

### Skin defenses & Microbiota balancing



Activation of TLR2 receptor (immunity): opportunistic pathogen detector



Activation of Dectin-1a receptor (immunity): opportunistic pathogen detector

*In vitro*



Commensal germ *S. epidermidis* in 2 weeks

*In vivo*



*S. epidermidis* / *S. aureus* ratio in 2 weeks

### Microbiota recovery after SLS impairment

*In vivo*

#### Commensal microorganisms

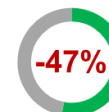
After impairment



Micrococcus



Paracoccus



Corynebacterium

7 days Phytosoothe<sup>®</sup>



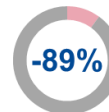
#### Pathogenic microorganisms



Pseudomonas




Pantoea



Acneic skin

Dry or stressed skin

A microscopic image of a plant root system, likely a ginseng root, showing a dense network of fine roots and larger, thicker roots. The roots are stained with fluorescent dyes, appearing in shades of orange, red, and green against a dark blue background. The overall appearance is that of a complex, branching structure.

**... and many more dermo-  
cosmetic actives in our  
pipeline!**

**Thank you**



**BASF**

We create chemistry

Care  
Creations™

