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# CASTALINE

Relieve your  
atopic prone skin

 **BASF**

We create chemistry

Care  
Creations™





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# CASTALINE



## From dryness to atopic prone skin

Key figures

Consumer needs

Existing solutions



## When nature comforts skin needs

By-product valorization of French chestnut tree



Strong *in vitro* demonstration on the 3 barriers of defense of atopic prone skin



Recovering skin confidence by managing and treating atopic prone skin





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## Strong in vitro demonstration on the 3 barriers of defense of atopic prone skin

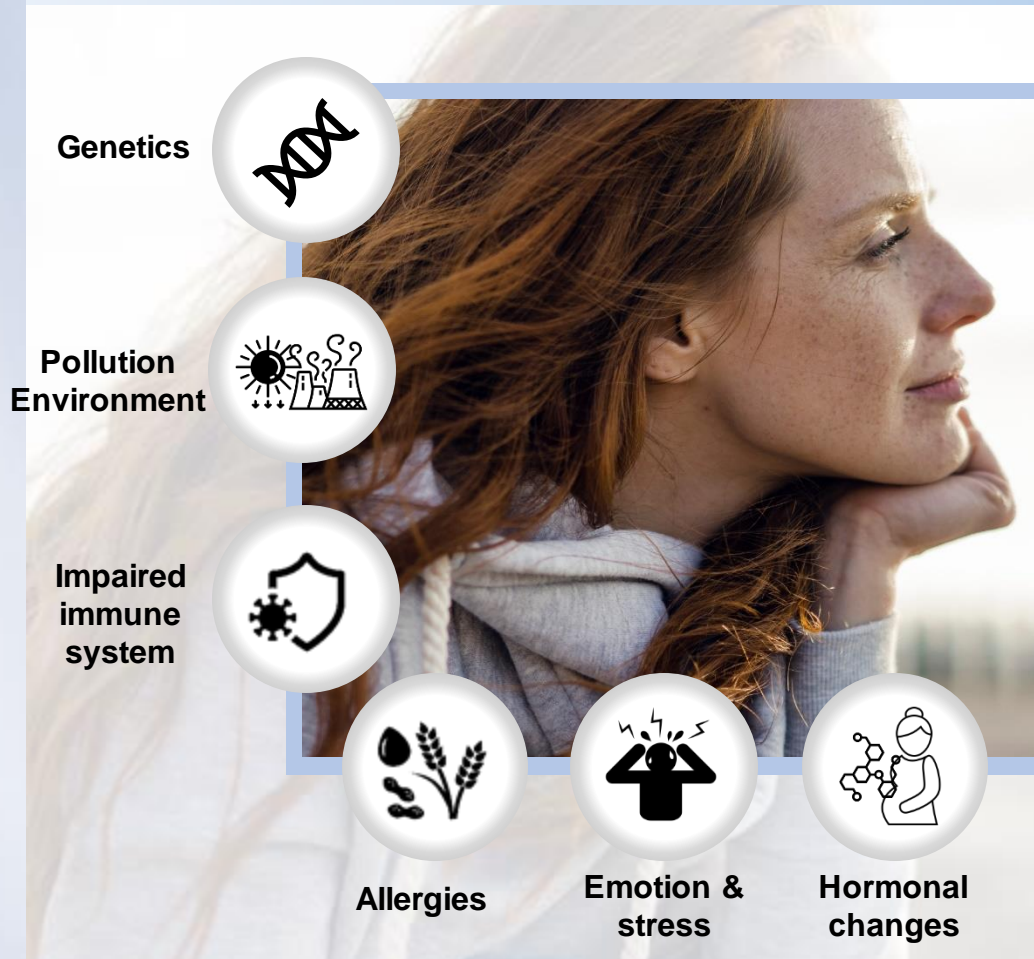


## Recovering skin confidence by managing and treating atopic prone skin

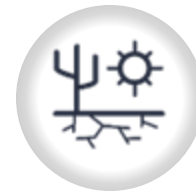
# Atopic Prone Skin

From dryness to atopic prone skin

## Causes



Dry and very dry skin is a **complex skin condition** due to **daily alteration of physical barrier** providing **discomfort, itchiness, irritation...** letting the skin becoming fragile.



**Extreme dryness**



**Intense itching**



**Red patches**  
often covered  
with small blisters

Without repairing and strengthening the skin barrier, it could **affect the microbial and immune barrier leading to atopic prone skin, or atopic dermatitis (AD)**, well-known as eczema



# Atopic Prone Skin

Physical impact...

Atopic dermatitis is an **inflammatory skin issue** that is characterized by **extreme dryness** and **red patches often covered with small vesicles** (small “blisters”) that cause **intense itching**.



Dry skin is particularly sensitive to its environment, with itchiness and redness



**9/10** daily suffer from **itching**.



AD affects **sleep quality** for more than **50%** of consumer (at least 5 nights/week)



For **77%**, feel **discomfort and pain** and **63%** have itching up to 12h/day



# Atopic Prone Skin

...and mental health impact



”Physically and emotionally is a tough journey, I was not confident enough to let someone get too close to me.”

Magali – 31 years old

Skin issue like atopic prone skin leads to a global exclusion from social life



French consumers<sup>(1)</sup> suffering from moderate to severe AD present **signs of stress for 83%** and **depression for 56%**



**45%** say AD has a negative impact on their **friendship** <sup>(1)</sup>



**68%**<sup>(1)</sup> of French consumers say that AD affects their **mood and their self-esteem**

[SOURCE: InfographieFrancaiseteczema ; Définition - Dermatite atopique (dermatite-atopique.fr)  
Les Français face à l'eczéma... De l'exclusion à la dépression - Sanofi France

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# Atopic Prone Skin

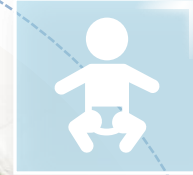
A complex skin condition affecting consumer all around the world

14% of Chinese consumers **have experienced dermatitis** in the last six months

14%

54% of UK consumers have **experienced dry skin** in the last 12 months, **18% eczema**

54%



**20%** of the world's child population is affected by eczema

**1/2** children is affected by the age of 5 years

**85%** of cases occur by the age of 5 years

70%

70% of patients are actively **looking for new solutions**

[SOURCE:: American Academy of Dermatology; French Society of Dermato-Pediatrics; EFA (European Federation Allergy & Airways) ; Pub Med.gov/Lightspeed/Mintel ; [Kantar Profiles/Mintel, April 2021](#)

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# Atopic Prone Skin

A strong growing market in all regions



**US**  
leader in AD treatment market followed by Europe, while Asia is set to be the fastest growth market for the category

**\$8.6bn**  
2020 Retail Value – Global

**\$21bn**  
AD market is projected to strike \$21bn in 2026

**13%**  
Retail value 2020-2025 CAGR

| Source: Mintel GNPD, <https://www.marketdataforecast.com/market-reports/atopic-dermatitis-treatment-market>



# Atopic Prone Skin

Skin characteristics comparison from normal to dry to atopic prone skin.



## NORMAL SKIN



**Physical barrier**



Intact skin possesses a strong physical barrier: moisture is kept in the skin



**Microbial barrier**



Hindered penetration of unwanted germs and allergens



**Immune barrier**



Skin reacts normally without inflammation issue



## DRY SKIN



**Physical barrier**



Disruption of cutaneous barrier: Moisture loss - Desquamation



**Microbial barrier**



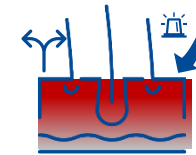
Disequilibrium between commensal and pathogen bacteria



**Immune barrier**



Skin reacts normally without inflammation issue



## ATOPIC PRONE SKIN



**Physical barrier**



Disruption of cutaneous barrier, penetration of allergens leading to erythema



**Microbial barrier**



Microbial superinfection, penetration of allergens



**Immune barrier**



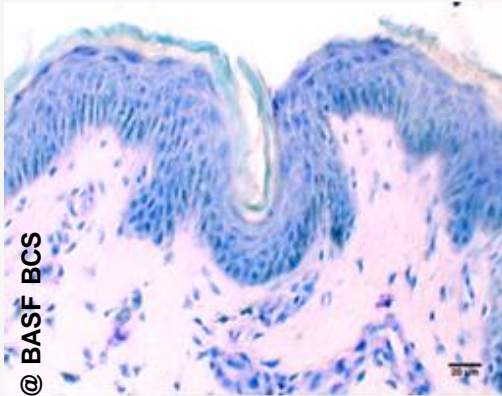
Invasion of inflammatory cells and inflammatory cytokines release

# Atopic Prone Skin

Skin characteristics of AD

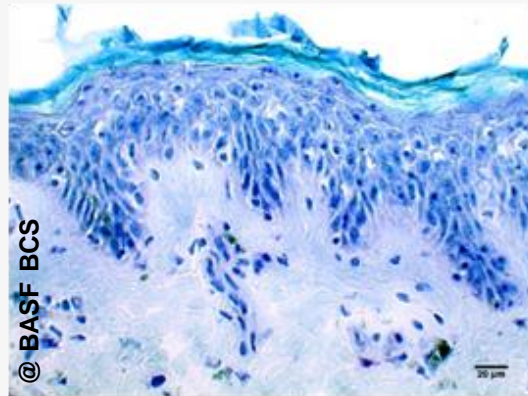
Human biopsy from a donor with severe atopic dermatitis

Normal Human Biopsy, woman, abdomen, 28 yo



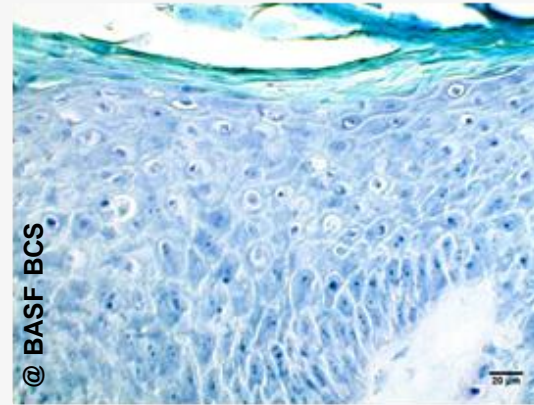
@ BASF BCS

Non Lesional Section (NLS)



@ BASF BCS

Lesional Section (LS)



@ BASF BCS

Toluidine staining

The epidermis is thicker in the LS area of the severe AD.

The upper layers of the epidermis are disorganized.



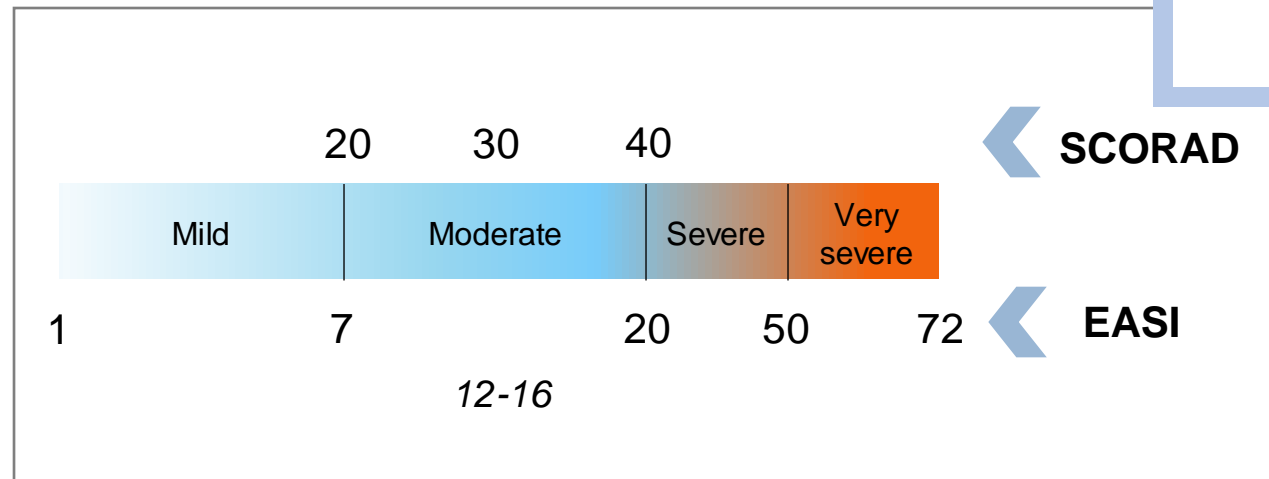


# Atopic Prone Skin

Skin evaluation

## Rating of the severity of atopic dermatitis:

- EASI score (*Eczema Area and Severity Index*)
- SCORAD score

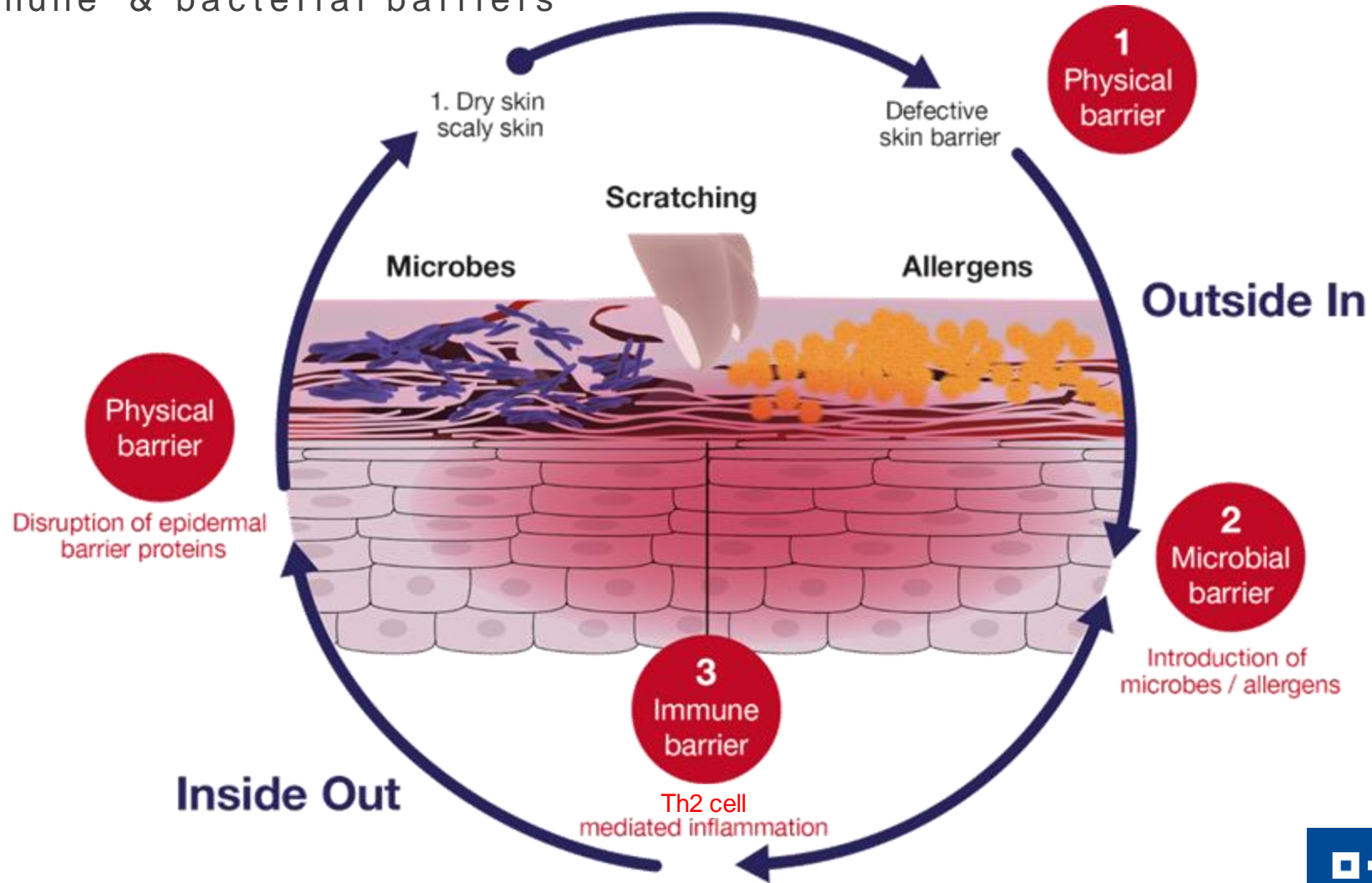


*The higher the score, the more the skin barrier is impaired, the skin is reactive.*

To evaluate the EASI Score, the dermatologist looks at **body areas**: Head, neck, trunk, upper and lower limbs, **area score** is recorded for each of the four regions. The area score is the percentage of skin affected by AD for each body region. **Severity score** is the sum of the intensity scores for four signs in each area: **Redness** (erythema, inflammation), **thickness**, **scratching** (excoriation), **lichenification**.

# Atopic Prone Skin

A vicious circle between impaired physical, immune & bacterial barriers





# Atopic Prone Skin

Skin characteristics through State of Art



**Increased permeability** (TEWL) of the *stratum corneum*, both in skin with or without lesions



**Structural abnormalities of the *stratum corneum*** such as decreased layer cohesion



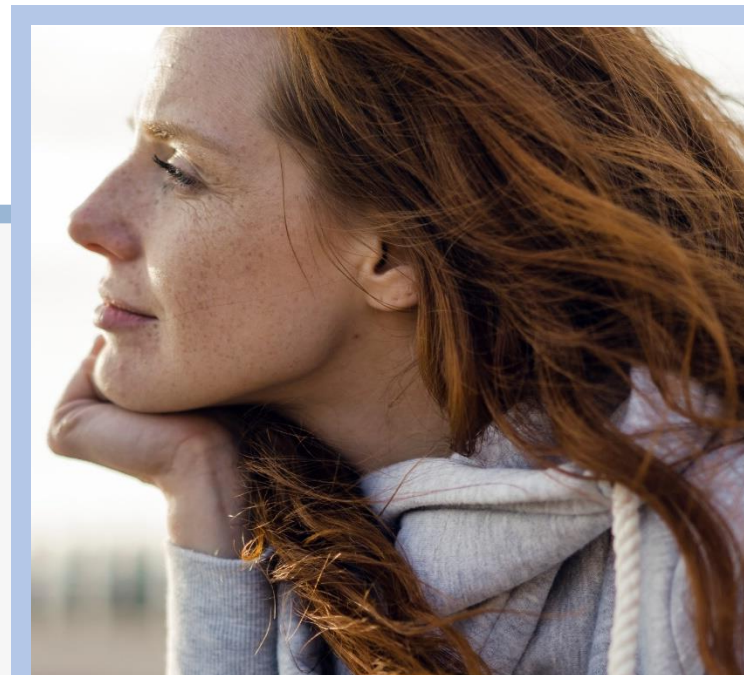
Reduced secretion of **lamellar bodies- Impaired of lamellar body traffic**, which are responsible for the formation of the cement



Proneness to bacterial (***Staphylococcus aureus***) infections, reflecting **an abnormal skin immune response** to microbes



Increased **pH value in the surface of epidermis**





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# CASTALINE



## From dryness to atopic prone skin

Key figures

Consumer needs

Existing solutions



## When nature comforts skin needs

By-product valorization of French chestnut trees



Strong in vitro demonstration on the 3 barriers of defense of atopic-prone skin



Recovering skin confidence by managing and treating atopic prone skin





# CASTALINE

Mild and natural  
solution to  
relieve atopic  
prone skin

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**Guardian of the  
Winter Gate  
*Castanea sativa***





# Castanea sativa

Well-known and reassuring chestnut tree with health properties



Chestnut tree

Native to Northern hemisphere, having long been cultivated and consumed throughout Asia, Europe and America. Chestnuts have been cultivated for at least 3,000 years in the Mediterranean region, and it is believed that the ancient Greeks introduced the European chestnut from Asia minor. The Romans were responsible for extending the cultivation into northwest and central Europe. Known to support dryness, and acid soil pH.



## Well-known properties

Anti-inflammatory, antibacterial, soothing. Known to relax muscles.



## Nutrition

Roasted European chestnuts are a source of phosphorus. Source of vitamin B,C and E, working on cell energy, contributing to growth and rejuvenation of tissue, and formation of red vessels.



## Medicinal uses

Anti-cancer properties, enhance therapeutic effects of conventional therapy for example, works on inflammation, helping patient to reduce fatigue after chemotherapy, boosting key immune cells.



## Ayurveda uses

Be suitable for people with rather frail physical state, who are often cold, feel tired and have a restless mind.

# Castaline

By-product valorization of French chestnut trees



Extract of **organic certified leaves** of chestnut trees

**Manually harvested** from August to September

Harvest **without impact on the preservation of the species** to create a new value stream in chestnut production

**By-product:** leaves are carefully collected from young trees that do not bear fruit

**Rich in flavonoids:** Astragalin and Miquelianin

**2 sourcings in France:** mainly Ardèche and Cher to ensure **traceability to the source and reliable supply chain**



## King of Tree

up to 30  
meters

# Castaline

## Product characteristics

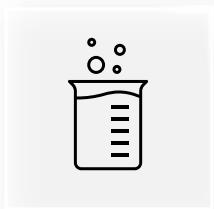
CASTALINE	BC10133										
Description	Natural extract of organic certified leaves of chestnut trees, characterized by Astragalin and Miquelianin										
INCI	Glycerin (and) Water (and) Castanea Sativa (Chestnut) Leaf Extract										
Dose of use	2 %										
Aspect	Syrupy liquid, dark yellow to amber with characteristic odor										
Solubility	Soluble in water										
Preservative system	None										
Naturalness content (ISO 16128)	100% natural origin, Organic farming, Cosmos certification in progress										
Regulatory data	<table border="1"><thead><tr><th>PCPC</th><th>IECSC</th><th>IECIC 2015</th><th>JP Cosmetics</th><th>JP QD</th></tr></thead><tbody><tr><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td><i>not listed</i></td></tr></tbody></table>	PCPC	IECSC	IECIC 2015	JP Cosmetics	JP QD	✓	✓	✓	✓	<i>not listed</i>
PCPC	IECSC	IECIC 2015	JP Cosmetics	JP QD							
✓	✓	✓	✓	<i>not listed</i>							





# Castaline

Formulation & storage conditions

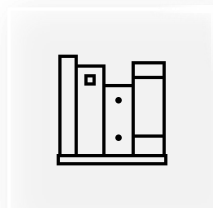


## Formulation method

Incorporated up to 80°C or at room temperature for a cold process.

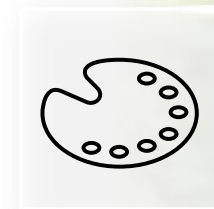
pH 3-7

OK at Room T°, slight color change at 45°C



## Storage conditions

In its packaging at 10-30°C  
Shelf life: 18 months



No  
Color impact





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# CASTALINE



## From dryness to atopic prone skin

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## When nature comforts skin needs

By-product valorization of French chestnut



## Strong *in vitro* demonstration on the 3 barriers of defense of atopic prone skin – 2D & 3D models

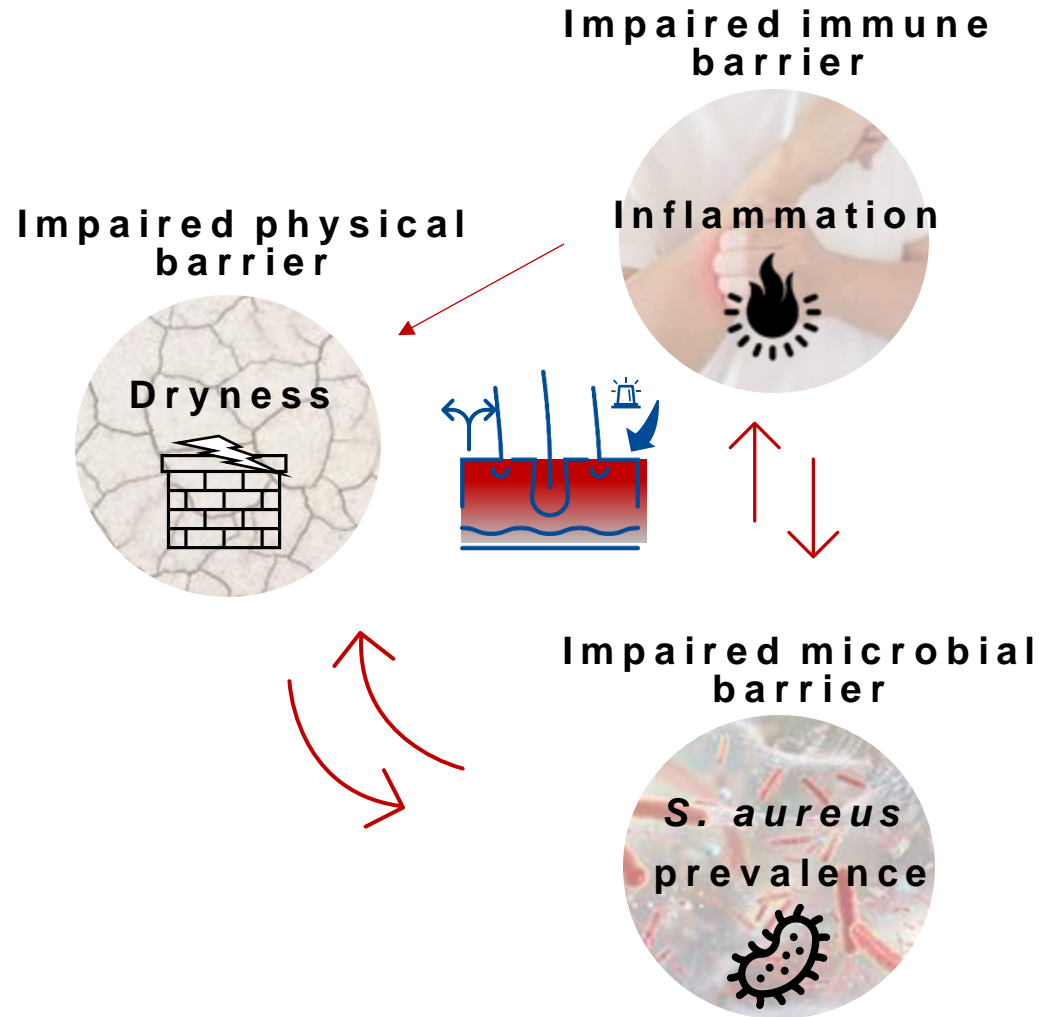


Recovering skin confidence by managing and treating atopic prone skin



# Castaline effect

A 3 defense-step action on skin barrier

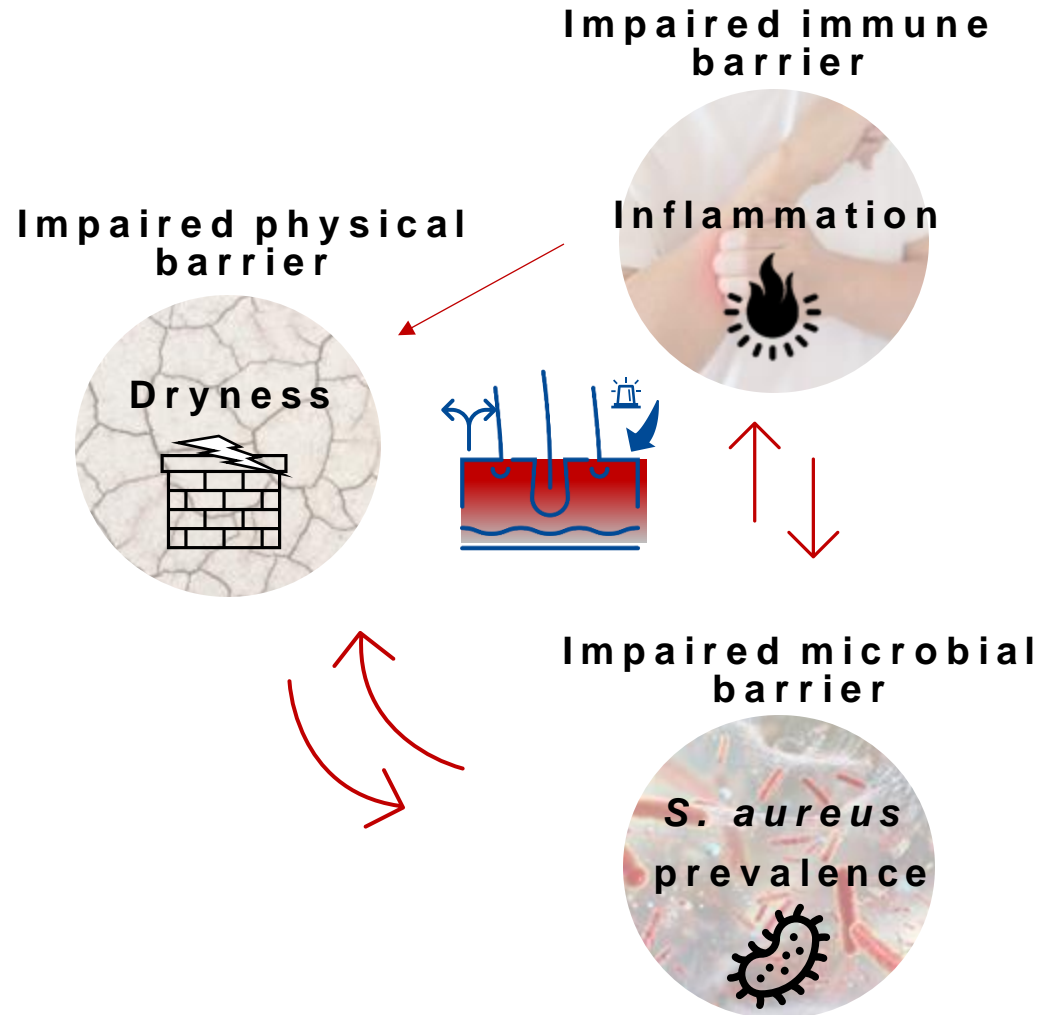




# Castaline on 3D models

Strong connection between inflammation and microbiome

What we know



Inflammatory cocktail **TH2 cytokines: IL-4, IL-13, IL-31** characteristic of the first acute phase of AD

TH2 cytokines also **facilitate *S. aureus* adhesion and colonization**



***S. aureus* worsens and prolongs the state of atopic prone skin** through virulence factors and generated-inflammation **and leads to a decrease of microbial diversity.**



# Castaline strong demonstration

Does inflammation favour the invasion of *S. aureus* ?

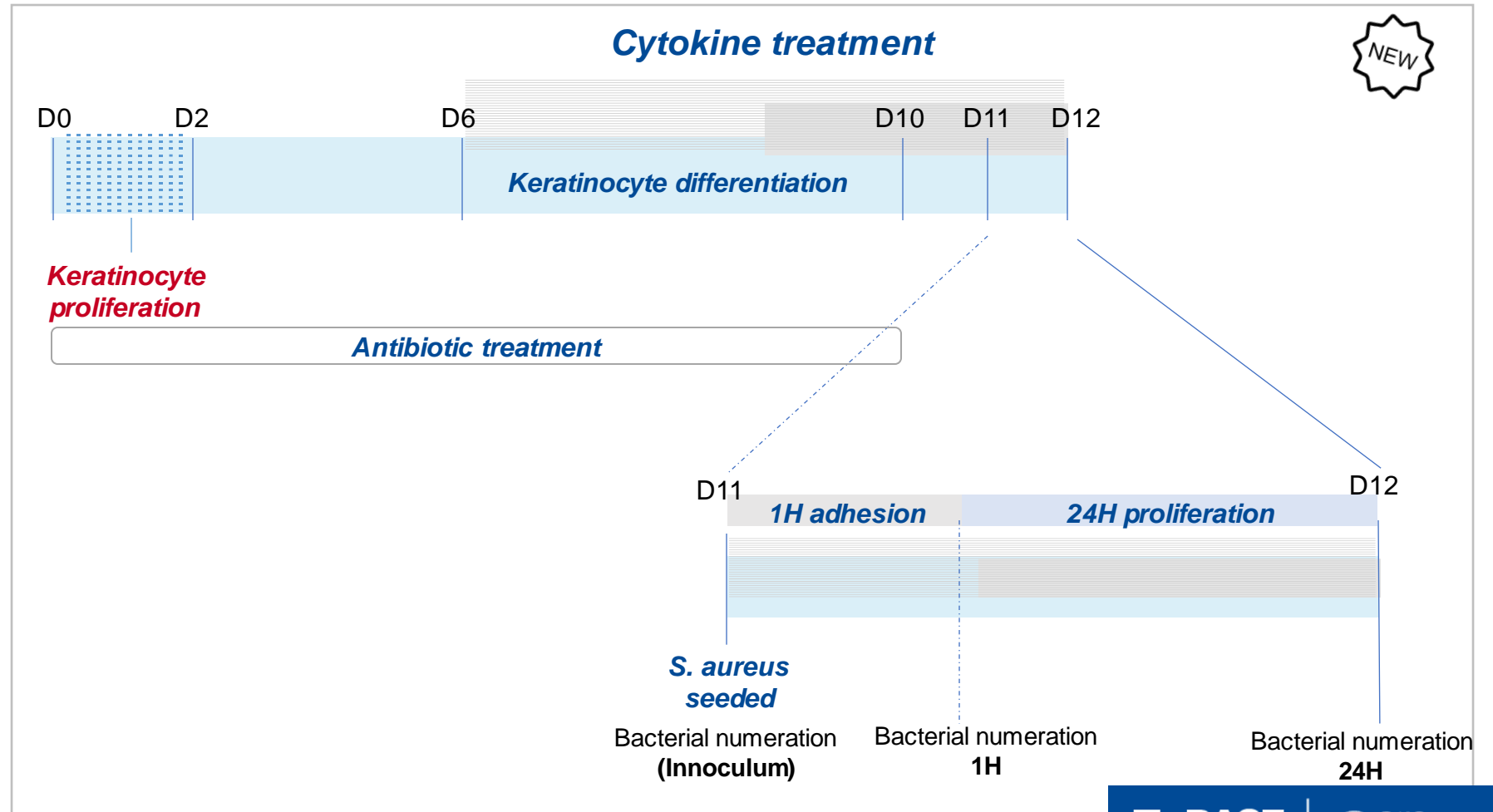
**Protocol of the reconstructed epidermis, 3D model, for bacterial numeration with or without the inflammatory cocktail C1:**  
**TH2 cytokines (IL-4, IL-13, IL-31) specific of acute AD and TNF $\alpha$**

**SA**

Without Infl. Cocktail\*: *S. aureus*

**C1+SA**

With Inf. Cocktail\*: C1 + *S. aureus*





# S. aureus

Inflammation favors *S. aureus* adhesion and growth



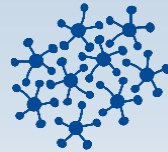
Adhesion %  
of *S. aureus*

up to 6 times

Inflammation allows a better *S. aureus* adhesion, up to 6 times more than in non inflamed RE.

At 1H, after having deposited the mother solution of bacteria-Counting.

- Non inflamed: 4% of bacteria adhere
- Inflamed: 18- 26% of bacteria adhere

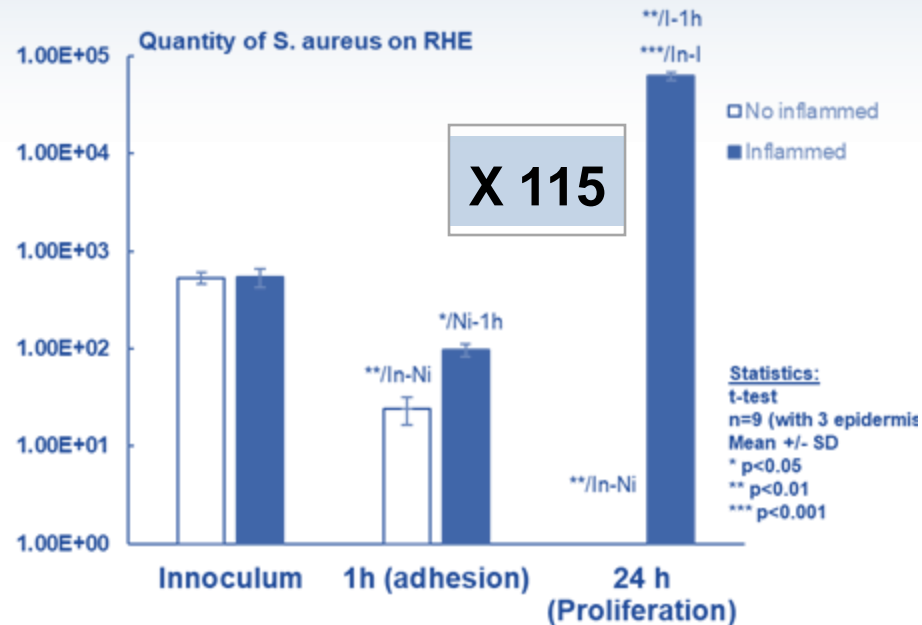


Count of *S. aureus*  
with time of culture

BCS  
discovery

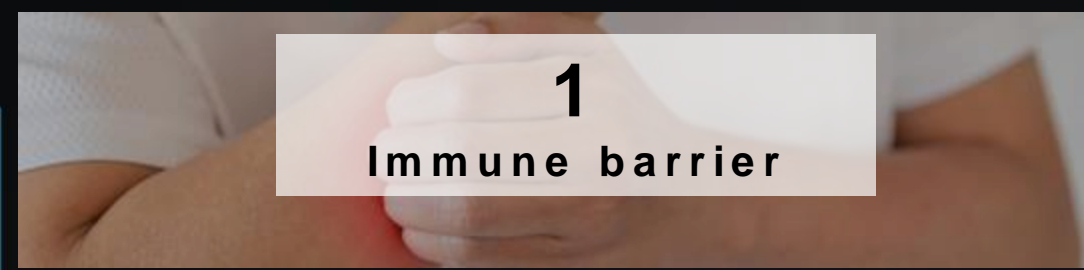
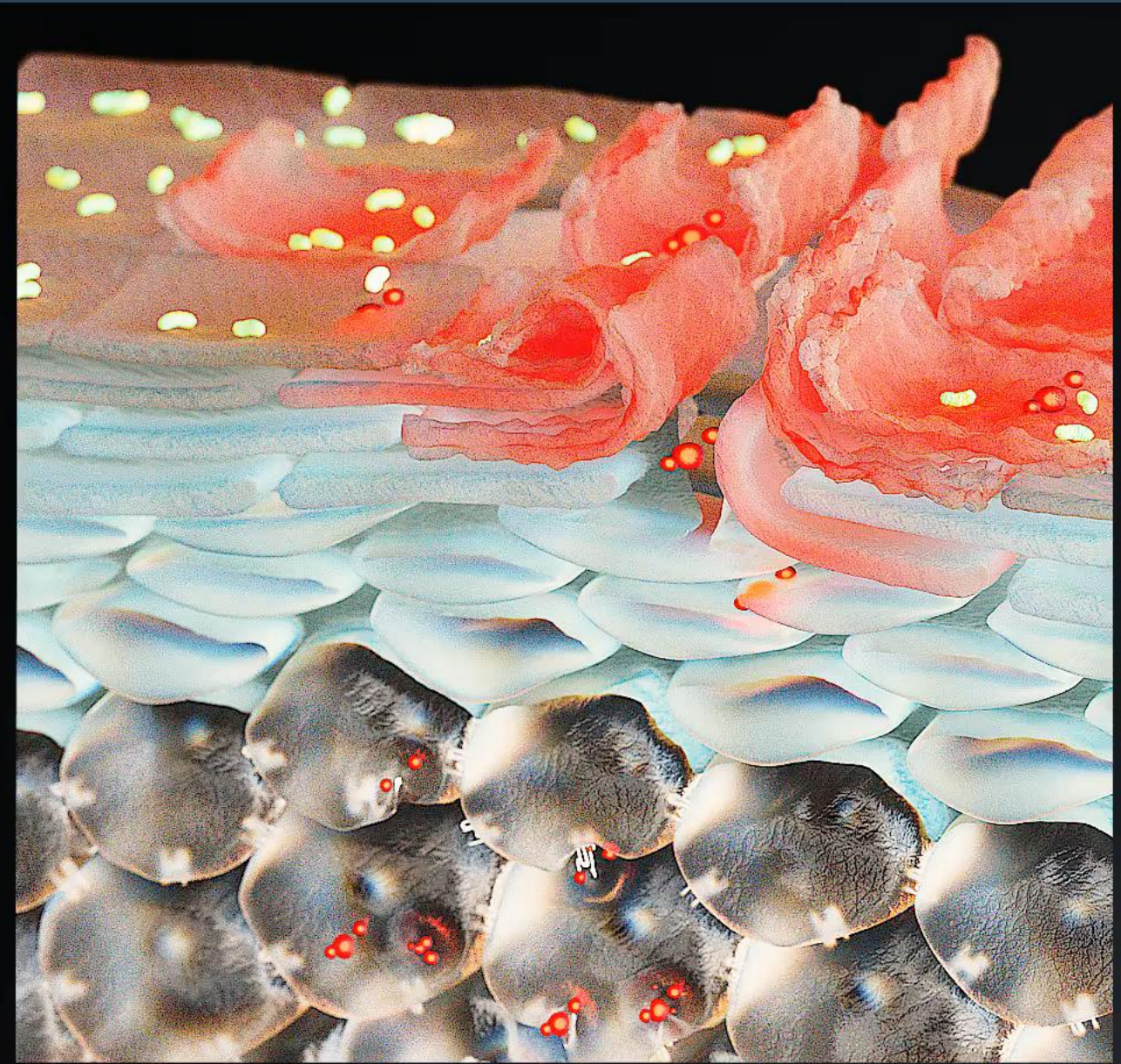


Without inflamed cytokines, *S. aureus* doesn't grow and even die.



Inflammation  
increases  
*S. aureus*  
adhesion  
up to 6  
and growth  
x115





1

Immune barrier



### Lymphocytes and Macrophages:

First skin defense line with TH2 cytokines: IL-4, IL-13, IL-31

- Downregulate terminal differentiation genes and tight junction products
- Facilitate *S. aureus* adhesion and colonization

### Keratinocytes:

2<sup>nd</sup> skin response: release of pro-inflammatory cytokines that amplify the process

# 1 - Castaline & immune barrier

Role in the reduction of inflammation in atopic prone skin



1

IMMUNE  
BARRIER



*S. aureus* is the key factor that increases IL-8 release with a moderate inflammation.



Castaline decreases inflammation even in presence of *S. aureus*

IL-8 : -30% \*\*\* p< 0.001

Castaline reinforces  
1<sup>st</sup> line of defense:  
macrophage

IL-8 : -55% \* p< 0.05

Castaline at 0.03%

Castaline reinforces  
2<sup>nd</sup> line of defense:  
keratinocyte

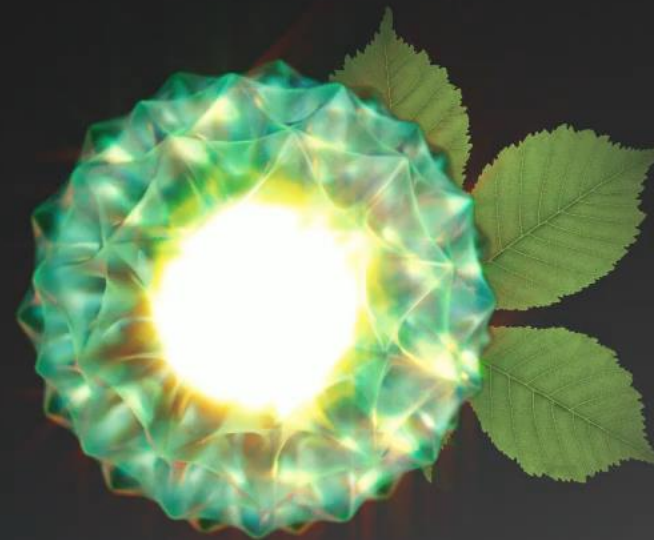
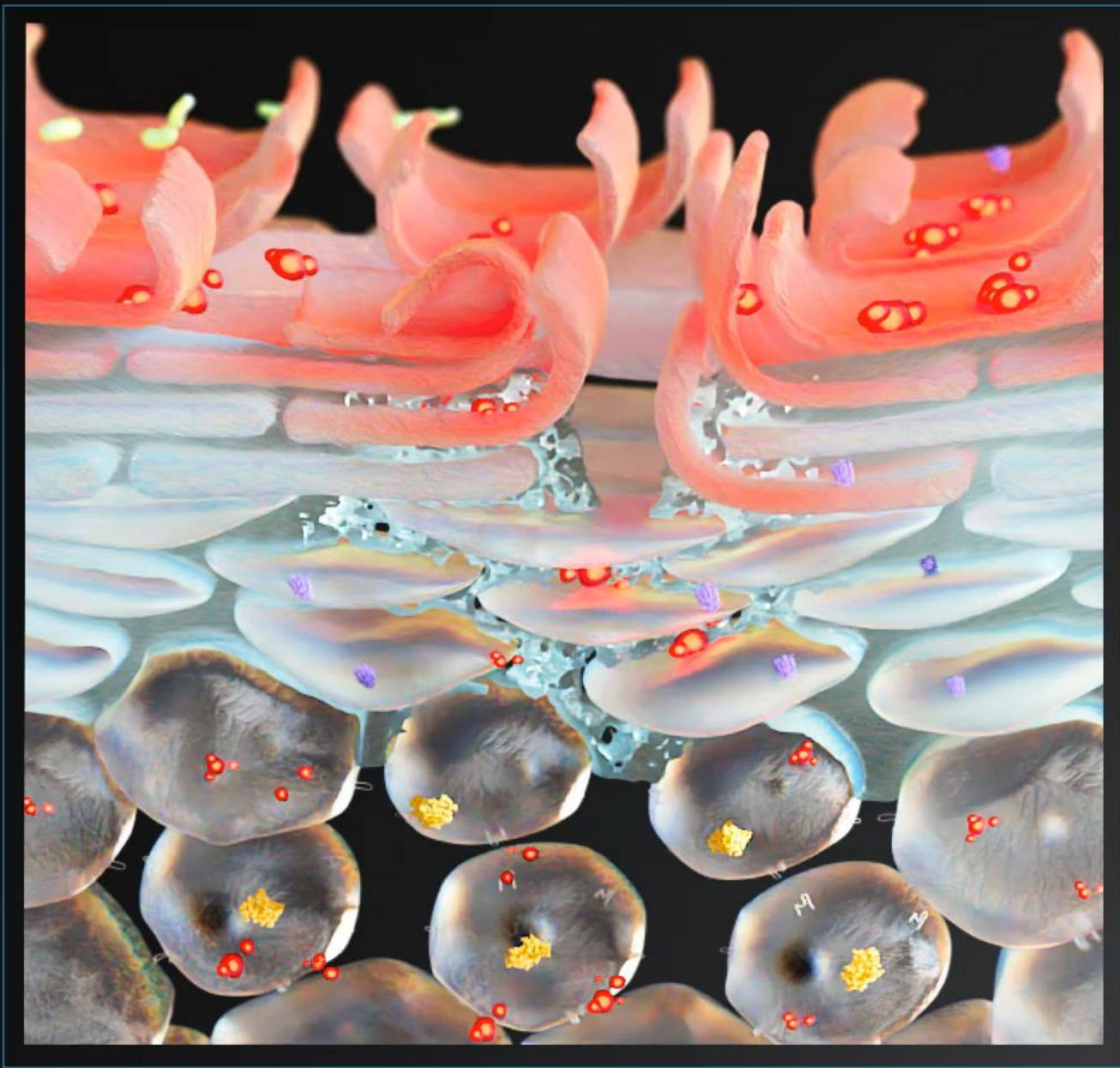
IL-8 : -76% \*\*\* p< 0.001  
IL-6 : -88% \*\*\* p< 0.001

Castaline at 0.03%

Prevent erythema  
Inflammation

Castaline significantly decreases inflammation even in presence of *S. aureus* at 2 level of defense of the skin

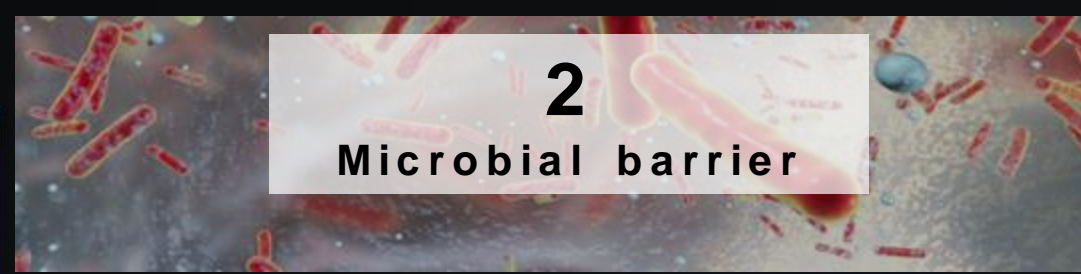




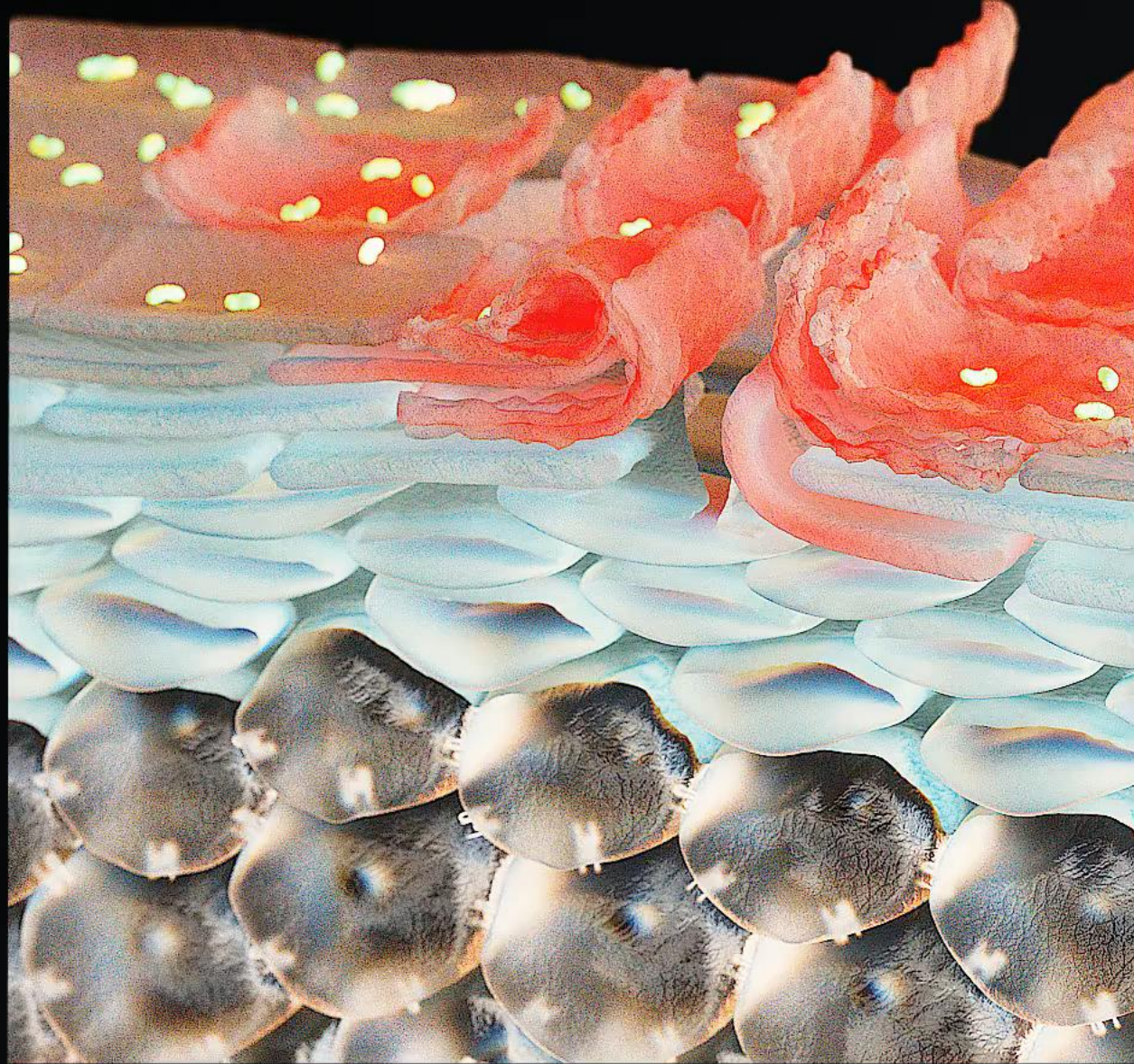
**Castaline™**

**Help to limit inflammation induced by  
pathogens and allergens**





## 2 Microbial barrier



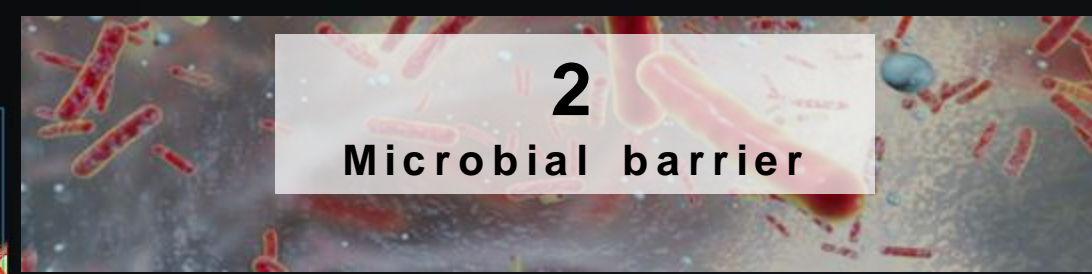
Atopic skin is characterized by an **over-colonisation of *S. aureus***, that can cause skin infection. Chronic skin damages will create a **favorable environment for enzymes useful for *S. aureus* invasion:**

- >Biofilm formation
- >Secretion of lipase
- >Hyaluronidase
- >Plasminogen activation

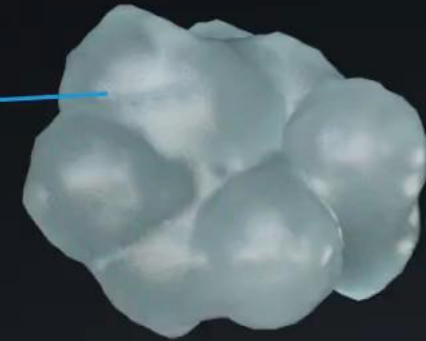


2

## Microbial barrier

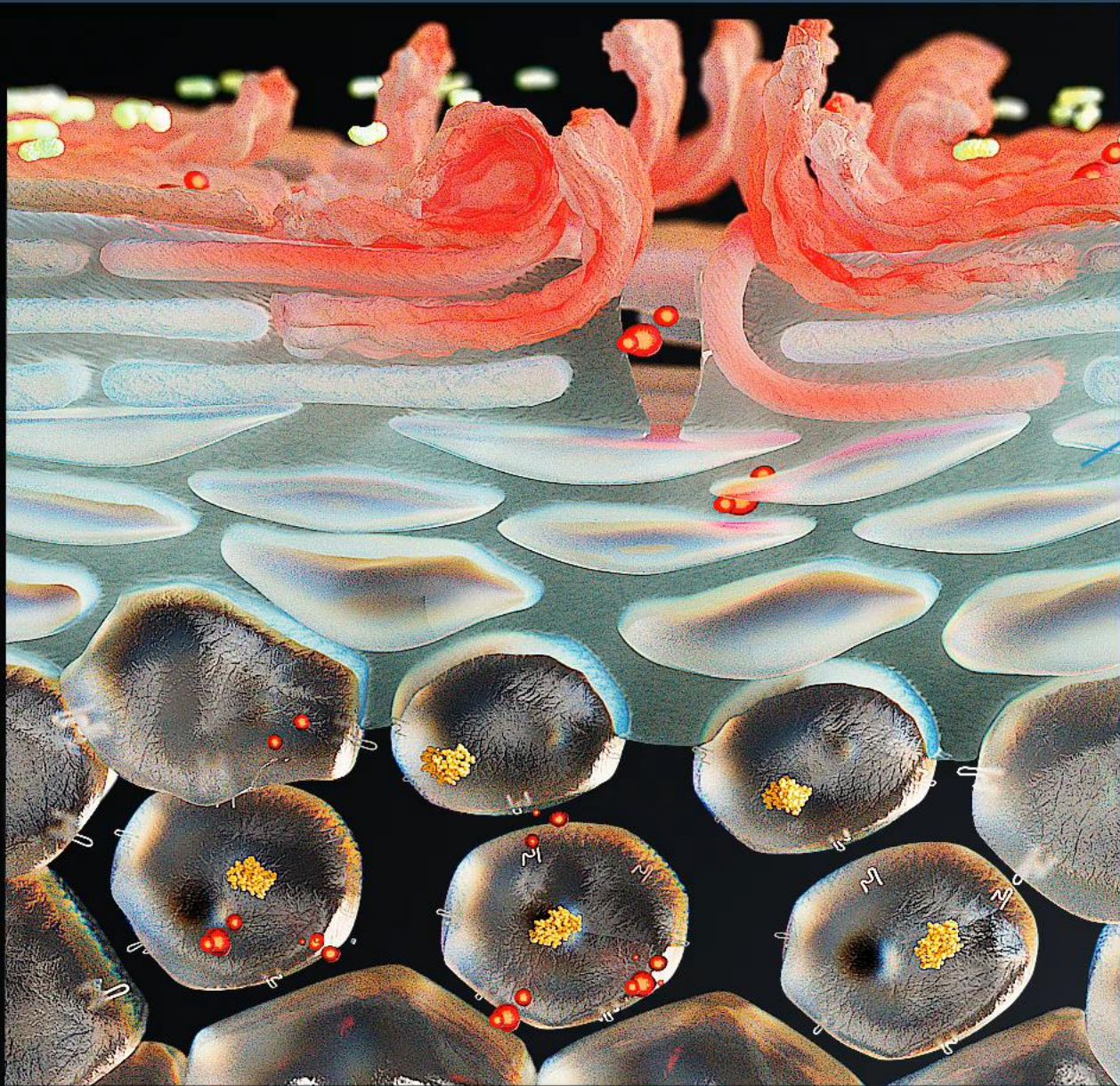


Lamellar  
body content



***S. aureus*** worsens and prolongs the state of atopic prone skin through virulence factors and generated-inflammation:

- Biofilm formation
- Virulence enzymes





# 2 - Castaline & microbial barrier

Role in *S. aureus* Biofilm formation inhibition and enzyme virulence reduction



2

MICROBIAL  
BARRIER

Impedence measurement: biofilm formation

**-100%** Castaline 1.5 %

Castaline reduces activity of enzymes  
useful for *S. aureus* invasion

**Lipase Activity**

known  
to release large  
amounts of fatty acids

**-86%**

Castaline 1.25 %

**Plasminogen  
Activation**

*S. aureus* activates  
plasminogen in plasmin  
which was demonstrated  
overactivated in AD

**-83%**

Castaline 0.05%

**Hyaluronidase  
Activity**

*S. aureus*  
hyaluronidase  
facilitates local spread  
of the infection

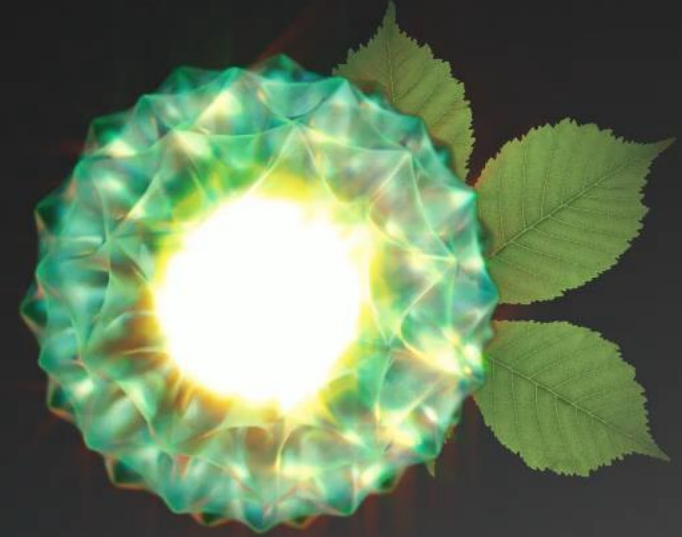
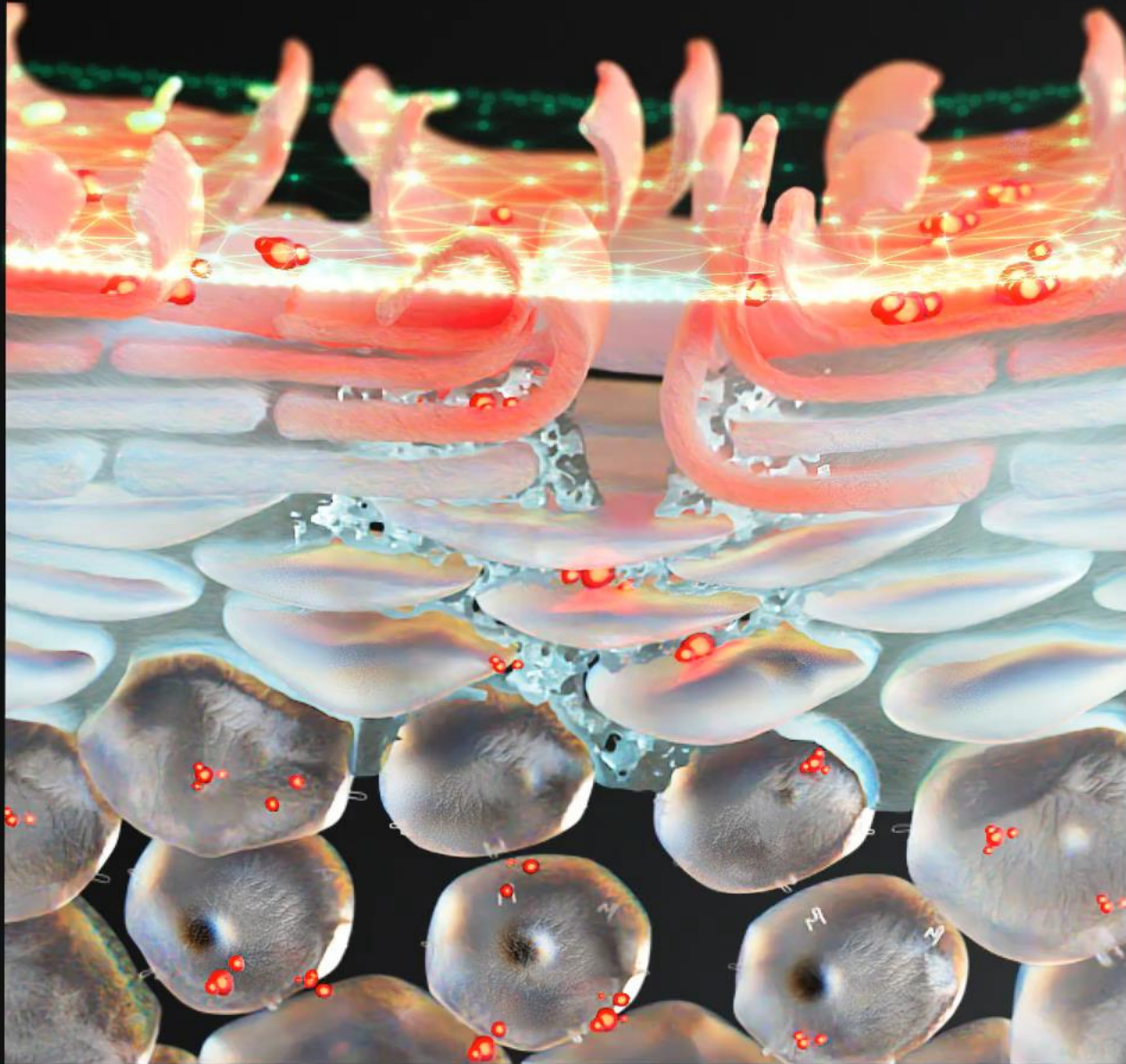
**-33%**

Castaline 1%

Prevent microbial  
over-infection

Castaline helps  
to inhibit  
adherence and  
biofilm  
formation of *S.  
aureus*, being a  
strong inhibitor  
of  
*S. aureus*  
virulence





**Castaline™**

Helps to reduce favorable environment for enzymes useful for *S. aureus* invasion and thus reducing *S. aureus* biofilm



### 3

## Physical barrier



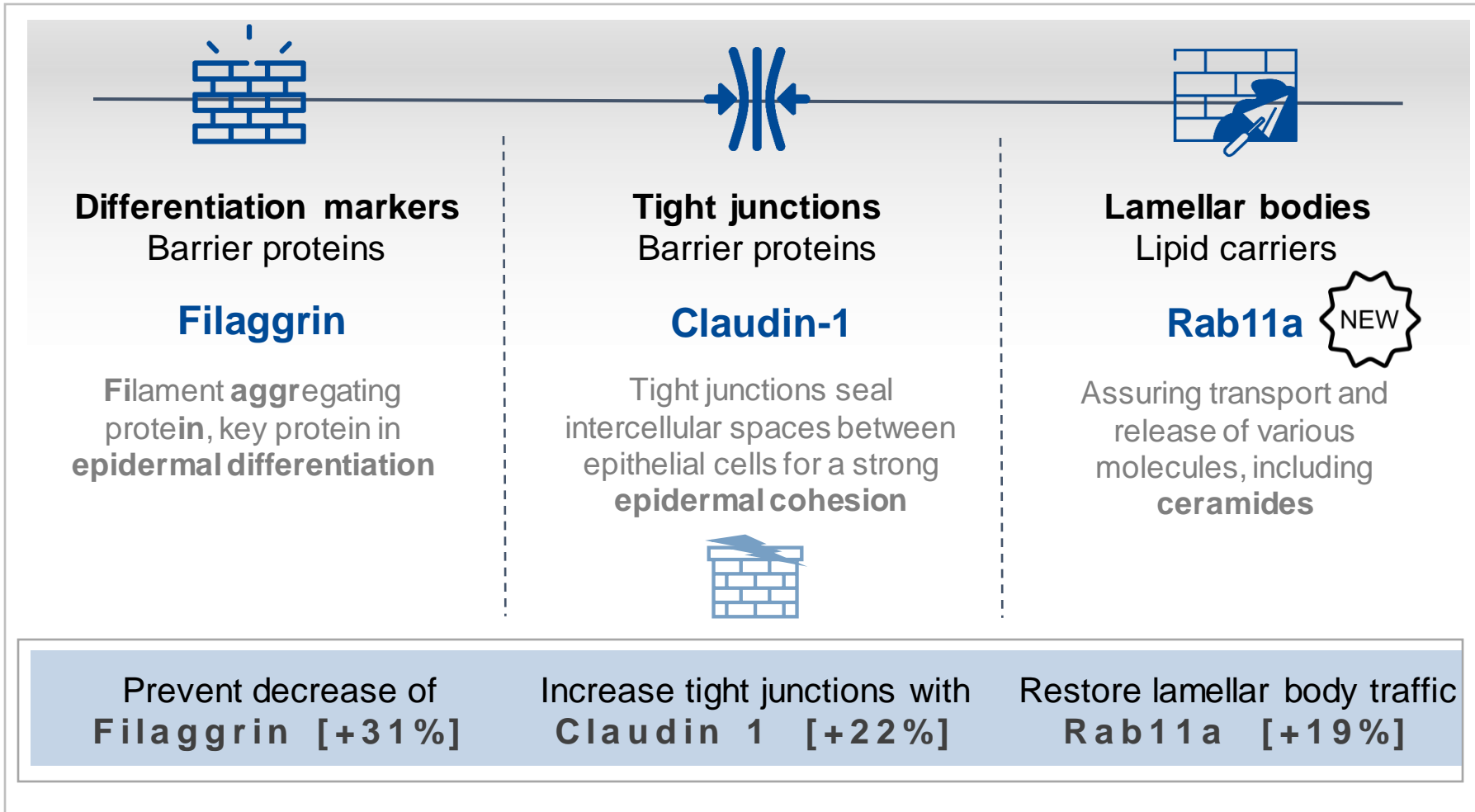
**Atopic prone skin is characterized by alterations and disorganization:**

- Epidermal proteins of differentiation
- Tight junctions' production and adherence
- Traffic of lamellar bodies (transporters of ceramides): to form the cement



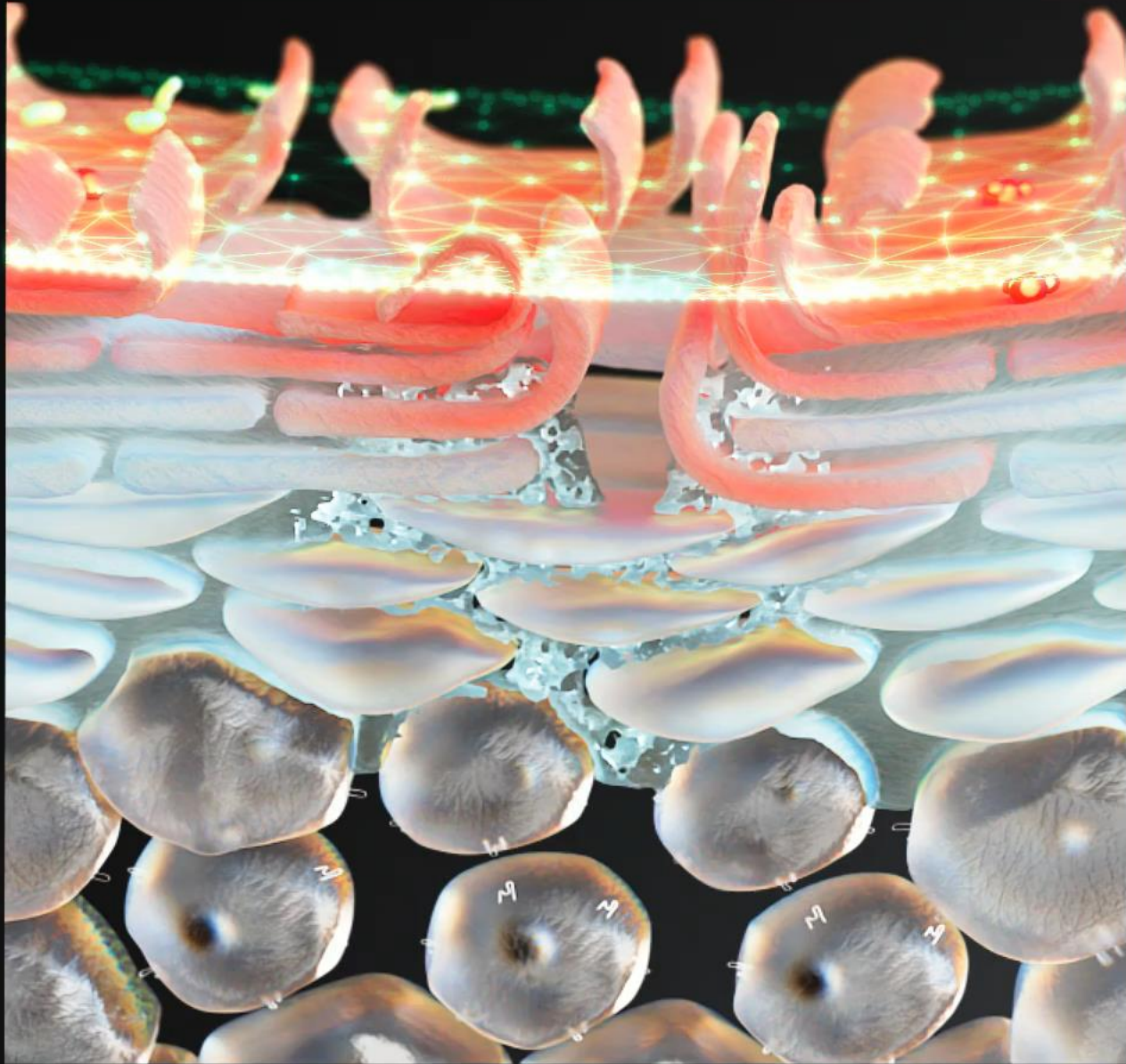
# 3 - Castaline & physical barrier

Demonstrated effect on the impaired physical barrier



Prevent impairment of physical barrier

Castaline helps to recover well organized and healthy skin barrier, to limit water loss and better protect skin



**Castaline™**

Helps to strengthen the physical barrier by increasing proteins of differentiation and cohesion and lamellar body traffic



# Castaline

Multifunctional mild solution to calm atopic prone skin



DELAY AD  
VICIOUS  
CIRCLE

MULTI-FUNCTIONAL  
STRONG IN-VITRO  
2D & 3D MODELS  
DEMO  
NEW BIO-MARKER



## IMMUNE BARRIER

**Reduce inflammatory cytokines: IL-8**

**-55%** in *S. aureus* stressed-macrophages, **-30%** in 3D model mimicking moderate AD

**Reduce inflammatory cytokines: IL-6 and IL-8**

**IL-8 [-76%] & IL-6 [-88%]** in *S. aureus* stressed-keratinocytes,



## MICROBIAL BARRIER

***S. aureus* virulence factors** : Biofilm formation **[-79%]**,  
Lipase **-85%** - Plasminogen **-83%** - Hyaluronidase **[-25%]**



## PHYSICAL BARRIER

- Prevent decrease of epidermal differentiation with **Filaggrin [+31%]**.
- Increase Tight junction with **Claudin 1 [+22%]** and Adherens junction with **E-Cadherin**
- Restore lamellar body traffic – **Rab11a [+19%]**



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# CASTALINE



## From dryness to atopic prone skin

Key figures

Consumer needs

Existing solutions



## When nature comforts skin needs

By-product valorization of French chestnut



## Strong in vitro demonstration on the 3 barriers of defense of atopic prone skin



## Recovering skin confidence by managing and treating atopic prone skin



# Castaline efficacy

## Clinical protocol



### Panel inclusion criteria

- 22 females and men / 18-66 years old
- EASI Scores: 3-11
  - 11 volunteers with EASI  $\geq$  7
  - 11 of them with EASI  $<$  7
- The dermatologist proposed to use **local EASI score** which concerns the studied lesion only (lesion on which the product is applied only).



### Test products (Ethic committee)

- Base cream emulsion
- Emulsion with 2% **Castaline**



### Application

- Double blind and randomized study, base cream controlled, on the left and right symmetrical sides of the body for 56 days

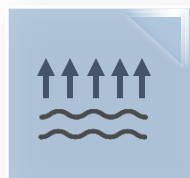


### Evaluation

- EASI Scores
- TEWL: (Tewameter TM 300)
- pH measurement
- Self assessment at D14 and D56
- Macrophotographs (Nikon D90)

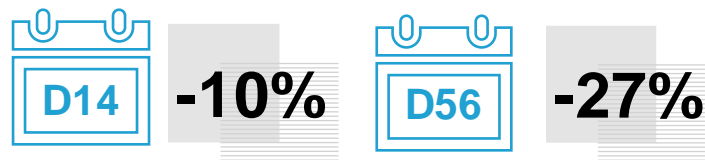
# Castaline efficacy

Clinical improvement of pH and TEWL  
And positive self assessment feedback



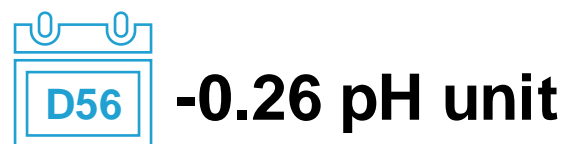
## Strong improvement of barrier over time

Significant decrease of TEWL vs baseline after 14 days,  
and vs base cream after 56 days (1.5 x better)



## Restoration of skin protective acid mantle over time

Significant decrease of pH after 56 days of treatment with  
Castaline at 2% while base cream has no significant effect.



Volunteer confirmed the  
improvement of their skin with  
time with use of Castaline 2%



82%

HYDRATION

73%

SOFTNESS

73%

SOOTHING



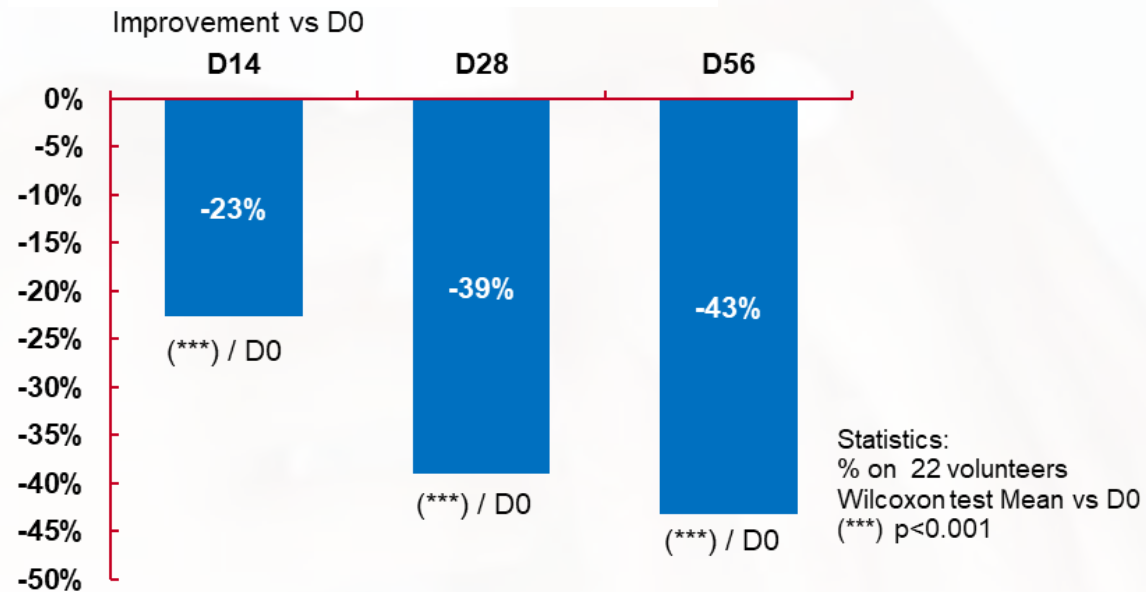
# Castaline efficacy

Clinical improvement of EASI Score



EASI  
SCORE

## EASI Score improvement vs D0



## Significant decrease of EASI grade with Castaline



-39%



-43%

- ✓ EASI score is improved with processing time
- ✓ Similar of base cream effect

**Dermatologist** evaluated a **significant improvement** at **D56** (86% base cream) for



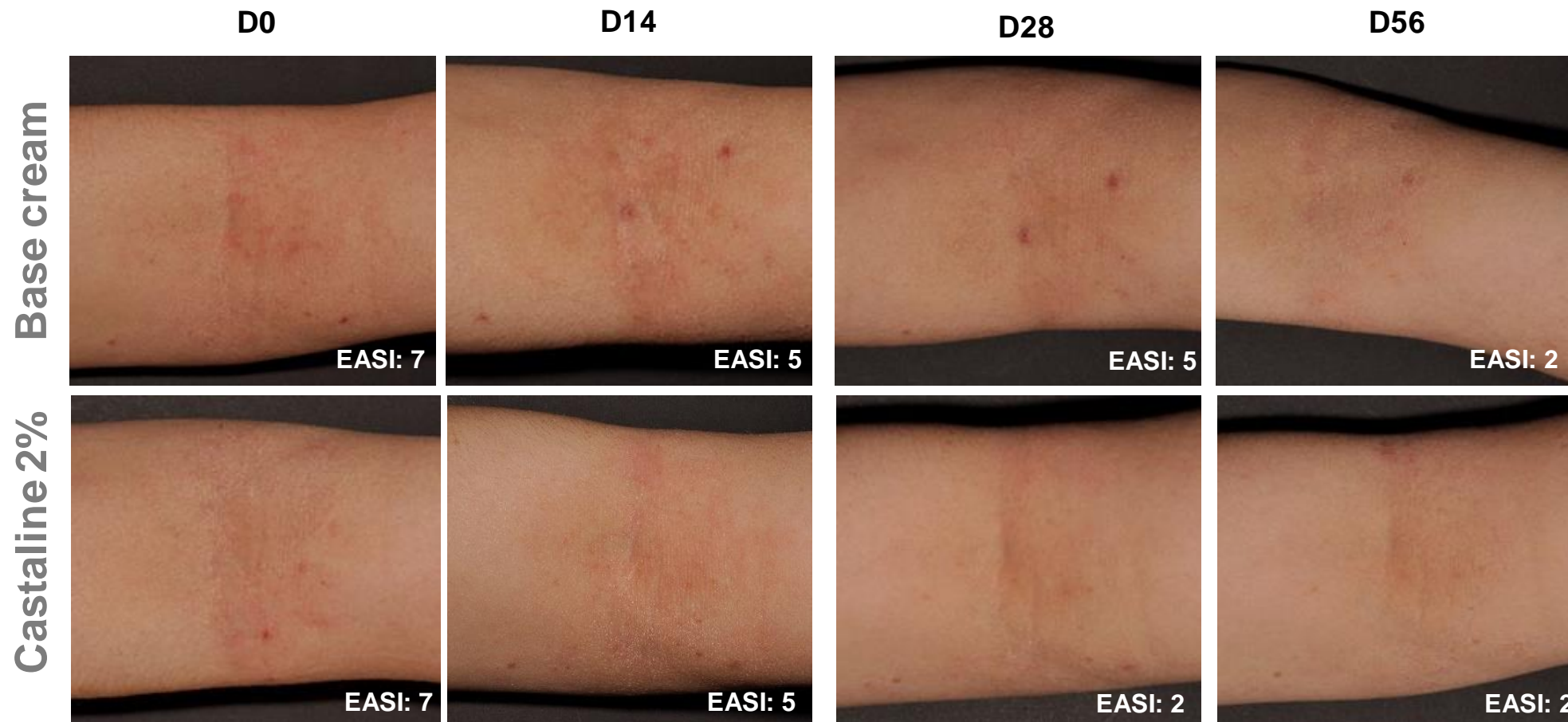
**86%** of volunteers

# Castaline efficacy

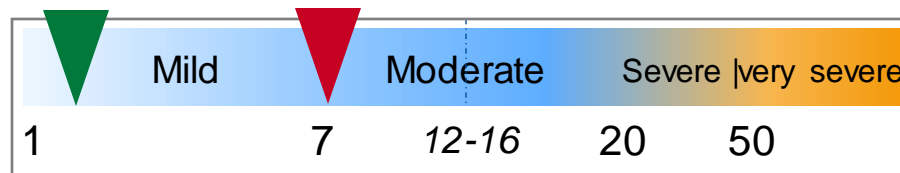
Clinical improvement of EASI Score on arm



EASI  
SCORE



IMPROVEMENT OF  
EASI SCORE





# Atopic Prone Skin

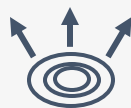
Skin characteristic covered by Castaline



Improve permeability (TEWL) : up to 27% after 56 days



Help to restore the structural abnormalities of the *stratum corneum* by increased layer cohesion (Filaggrin +31%, Claudin +22%)



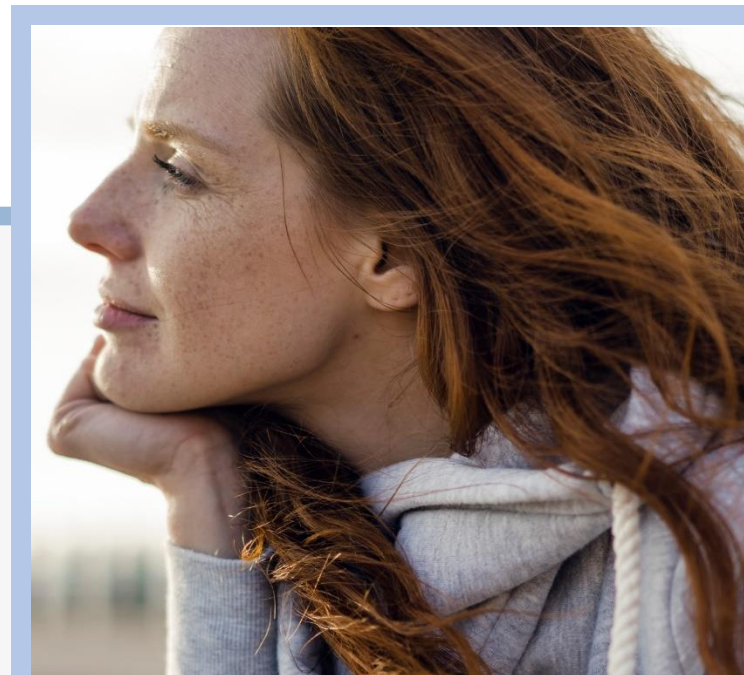
Increase secretion of lamellar bodies: Rab11a +19%



Acts on bacterial (*Staphylococcus aureus*) infections, improving skin immune response to microbes: up to 95% of *S. aureus* + decrease of inflammation (IL-8 -76%)



Decrease of pH value in the surface of epidermis (-0.26 pH unit)



## CONCEPT

# HYDRA BIOME ATOPIC SKIN RELIVER

NUTRI SOOTHING BODY  
BALM

## OILY COMPLEX

restore hydrolipid film, nourish  
the skin and avoid dehydration



## Castaline®

nutri *Castanea  
sativa* leaves  
extract to relieve  
DA

## Nutri-Soothing Body Balm

which protect atopic prone skin  
from itchiness, redness and  
creasis. Its formulation enriched  
with a french local castanea  
leaves extract and a soothing  
oily complex highly tolerate by  
atopic prone skin, the  
formulation restores the skin's  
barrier function and the acidic  
barrier for a healthier and more  
comfortable skin.

Balance of  
microflora

Soothing and anti-itching

Reduce signs of DA





# CASTALINE

## Local and responsible sourcing

From *Castanea sativa* leaves, manually harvested in France

## Organic certified

Highly innovative **3D skin model** mimicking mild to moderate atopic dermatitis

**The relief of atopic prone skin**, thanks to demonstrative *in vitro* results: **on the physical, immune and bacterial barriers: multiple actions in the vicious circle of Atopic prone skin.**

Incorporated into a formula able to improve the signs of atopic-prone skin, **Castaline restores the skin's barrier function and the acidic barrier for a healthier and more comfortable skin.**

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