

From epigenome to exposome: new perspectives in dermo-cosmetics

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International research collaboration projects

The Human Genome Project



What is the human genome sequence?

80 -90's

The Human Epigenome Project



How to explain so many differences?

2000's

The Human Exposome Project



What are our genes and organisms exposed to?

2010's

The Human Genome Project

>> International research effort to **sequence** and **map** the entire human genome



>> 1990: project formally **launched** (initiated in 1988)

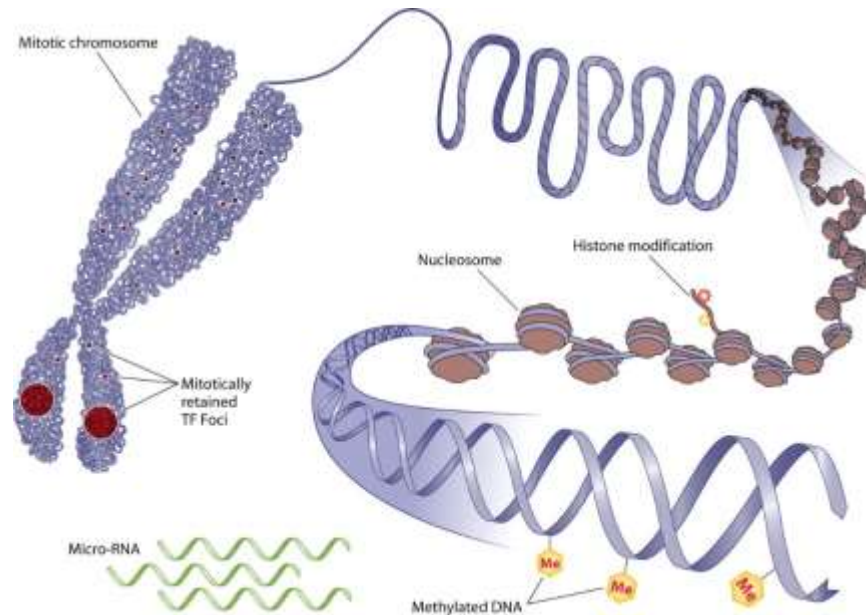
>> 1998: competition with a **private** approach (Celera Genomics)

>> 2001 : **first draft** of the human genome (Nature)

>> Project declared **finished** in 2003, two years ahead of schedule

The Human Epigenome Project

>> Epigenetic : heritable modifications of genes that **affect gene expression** but do not alter the DNA sequence



>> Aim of the project : identify **Methylation Variable Positions** (MVPs) in human genome

The Human Exposome Project(s)

>> 'Genetics load the gun but **environment pulls the trigger**'¹

>> **HELIX**: The Human Early-Life Exposome: how **early-life** environmental exposures impact child health across Europe

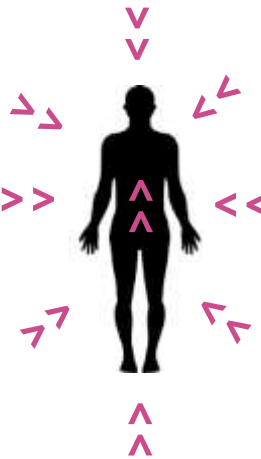
>> **EXPOsOMICS**: Programme which focuses on the effects of **air pollution** and **drinking water contaminants**

>> **HERCULES**: provides key infrastructure and expertise to develop and refine **new tools and technologies** to generate **exposure data** and improve metabolomics approaches

¹ Dr. Francis Collins, Director of the U.S. National Institutes of Health (NIH)

Exposome: an overview

- >> Firstly proposed in 2005 by Dr. Christopher Wild, a cancer epidemiologist
- >> Totality of (non-genetic) **exposures** to which an individual is subjected from conception to death, **complementing the genome**
- >> Three overlapping domains within the Exposome:



- **General external environment:** Urban environment, UV, education, climate factors, stress, blue light (380 - 500 nm)
- **Specific external environment:** specific contaminants, radiation, infections, lifestyle factors (**tobacco**, alcohol), diet, physical activity
- **Internal environment:** internal biological factors such as metabolic factors, hormones, gut microflora, **inflammation**, **oxidative stress**

Exposome and skin

Lifestyle and environment would age faster than genes

"Exposome would be responsible for 80% of premature ageing"¹

¹ Effect of the sun on visible clinical signs of aging in Caucasian skin - Clinical, Cosmetic and Investigational Dermatology, 2013



"Each individual possesses his own Exposome"²

²Thierry Passeron - professeur de dermatologie et chercheur à l'Inserm (Nice)

Jean Krutmann, Anne Bouloc, Gabrielle Sore, Bruno A. Bernard, Thierry Passeron

Journal of Dermatological Science, March 2017

Through new opportunities in Cosmetic industry ?

Current "Product approach"



The "Exposome shield" approach

>> Slimming

>> Revitalizing

>> Pore treatment

>> Moisturizing

>> Anti-oily skin

>> Scrubbing

>> Repairing

>> Remodeling

>> Skin complexion

>> Eye contour

>> Firming

>> Anti-wrinkle

>> Acne



>>ROS

>> Infections

>> Alcohol

>> Gut microflora

>> Physical activity

>> Stress

>> Climate factors

>> Diet

>> Tobacco

>> Education

>> Radiation

>> Lifestyle

>> Inflammation

>> metabolic factor

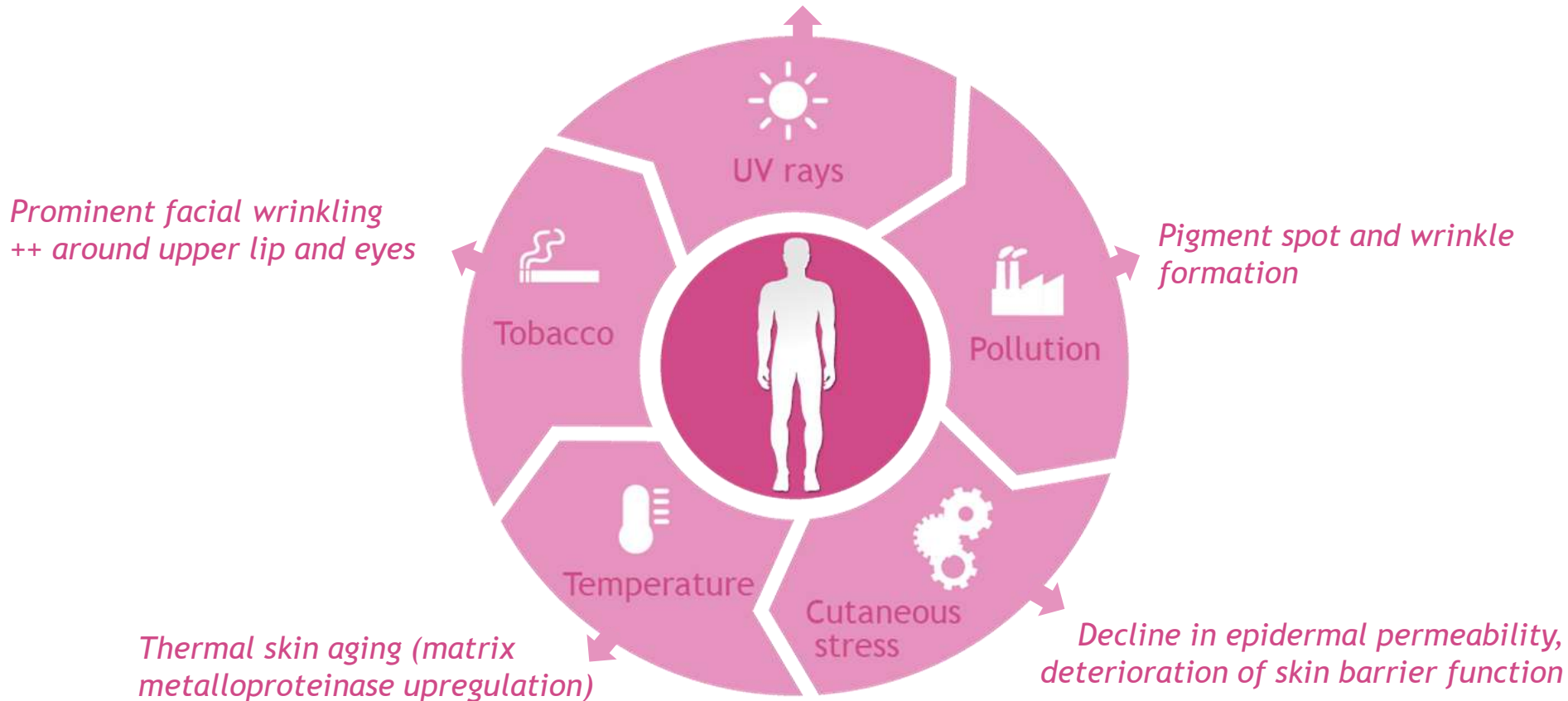
>> Hormones

>> Urban environment



Exposome and skin ageing

*Photoaging results from daily exposure (low doses)
→ long wavelength UVA1 is a major contributor*

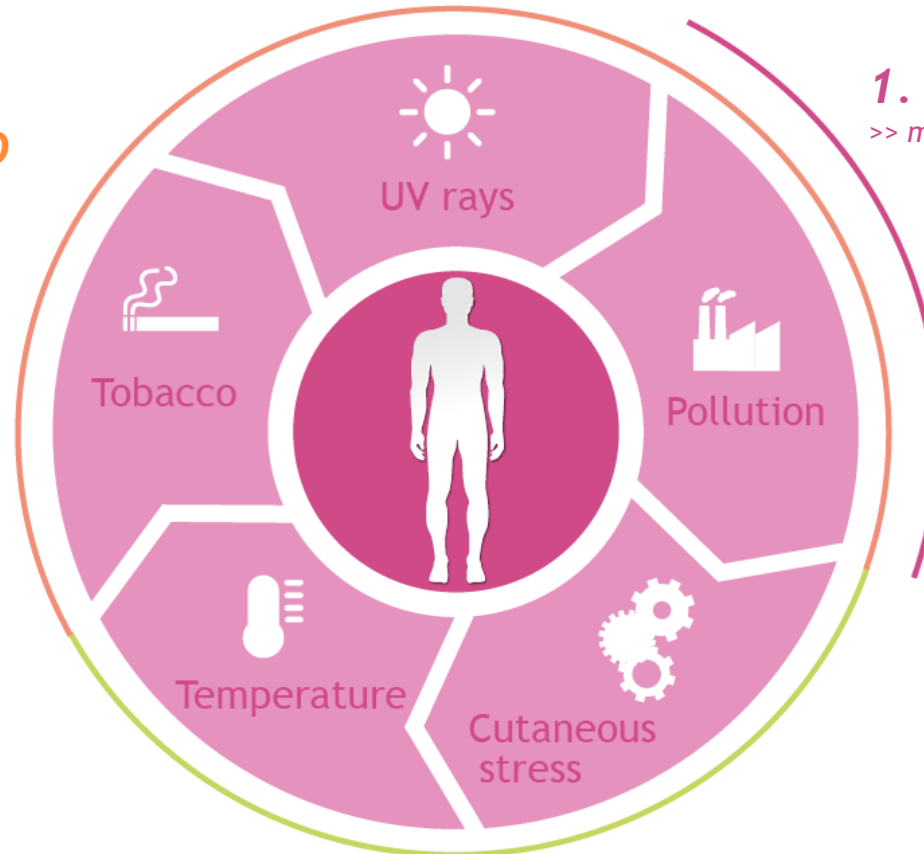


*Ref : Jean Krutmann, Anne Bouloc, Gabrielle Sore, Bruno A. Bernard, Thierry Passeron
Journal of Dermatological Science, March 2017*

Three botanical shields

2. BIOLOGICAL SHIELD

>> buckwheat seeds



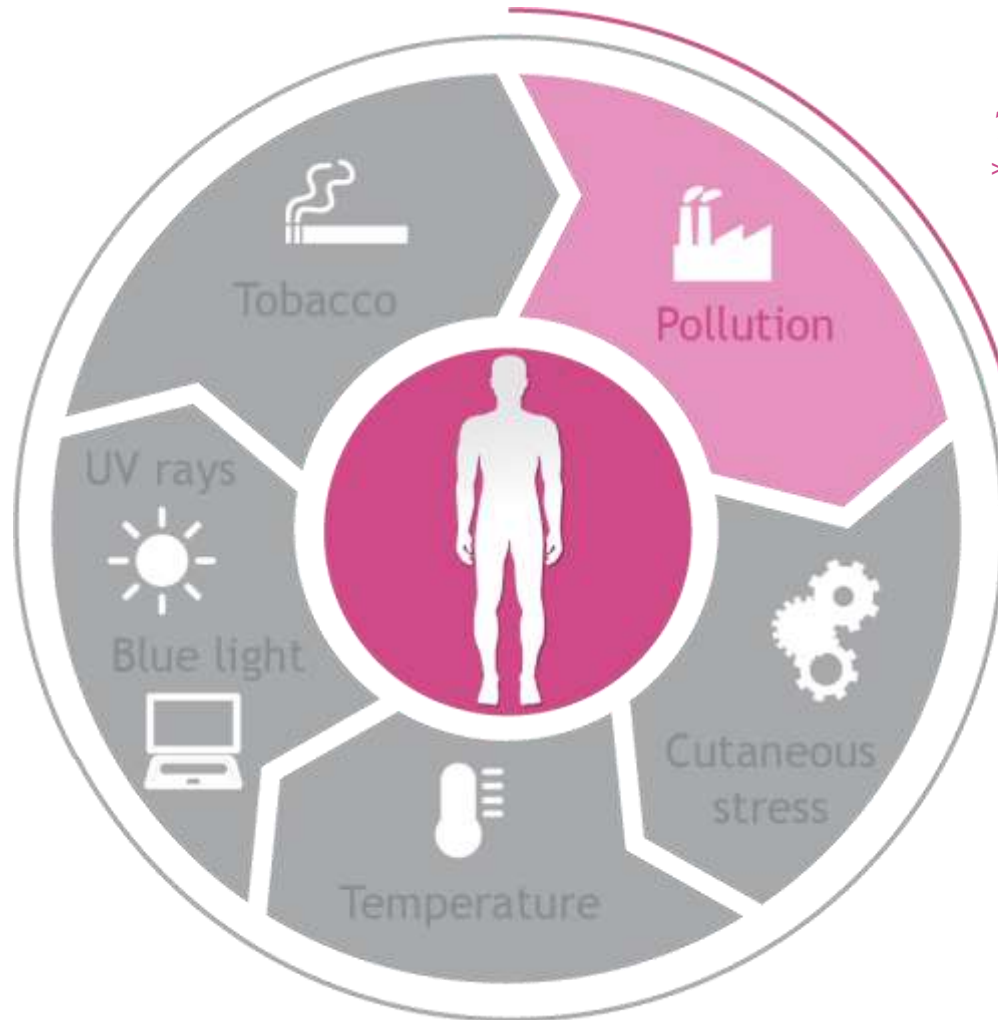
1. MECHANICAL SHIELD

>> marshmallow roots

3. SOOTHING SHIELD

>> saffron flower

Three botanical shields



1. MECHANICAL SHIELD

>> marshmallow roots

Osmo'city: Marshmallow



>> *Althaea officinalis*

>> Comes from the Greek (althein), "to heal"

>> Traditionally: for irritation of mucous membranes

>> Candy: traditional confectionary with the root

>> Rich in mucilages & polysaccharides

>> Marshmallow, a natural source of cocooning and enveloping substances ?



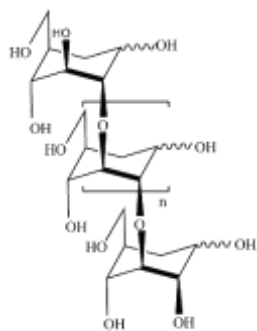
Osmo'city : Study of complex sugars



>> Determination of the average molecular mass of polysaccharides on root extract $\approx$ 32 kDa

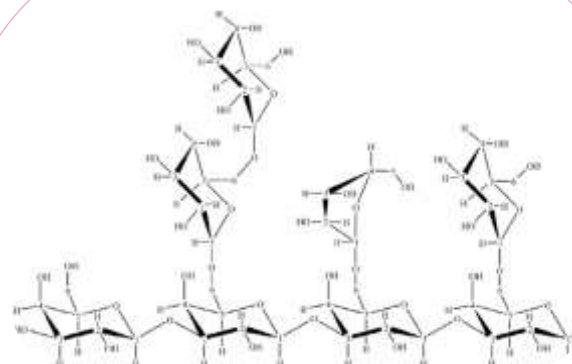
>> Determination of the GLYcoPROFILE

>> Potential characterisation of **glucans** and **arabinogalactans** known to create an **interaction with the skin cells** to create a **protective shield**



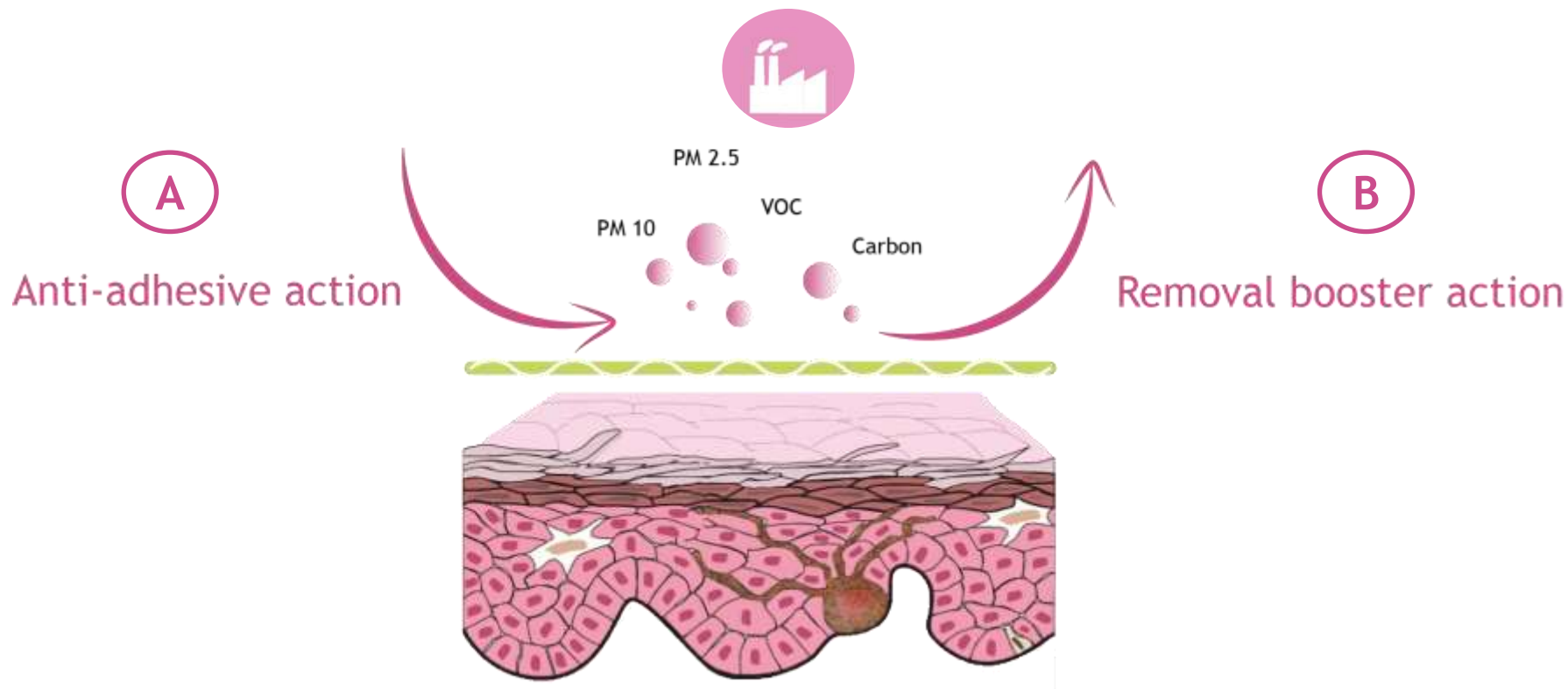
Poly(epoxy glucose)

Example of glucan



Example of arabinogalactan

Preventive and curative effects

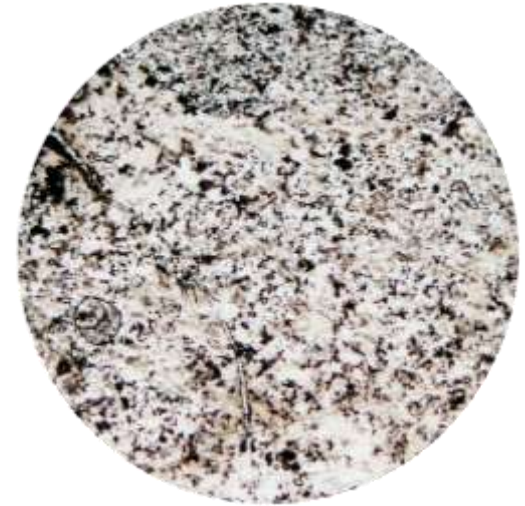


Anti-adhesive action

Shot after rinsing



Placebo gel + application of carbon particles on skin explants



Osmo'city® gel (3%) + application of carbon particles on skin explants

Inhibition of adhesion up to -18%*

>> Osmo'city protects the skin with a botanical non-occlusive protective film

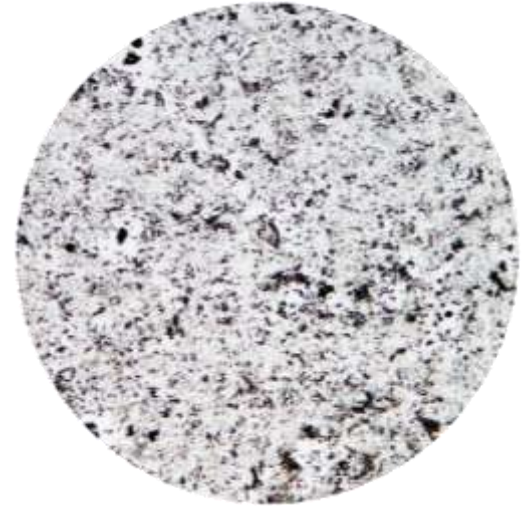
* significant $p < 0,05$

Removal booster action

Shot after rinsing



Application of carbon particles + **placebo**
rinsing solution on skin explants



Application of carbon particles + **Osmo'city®**
rinsing lotion (3%) on skin explants

Ability to remove particles up to -29%**

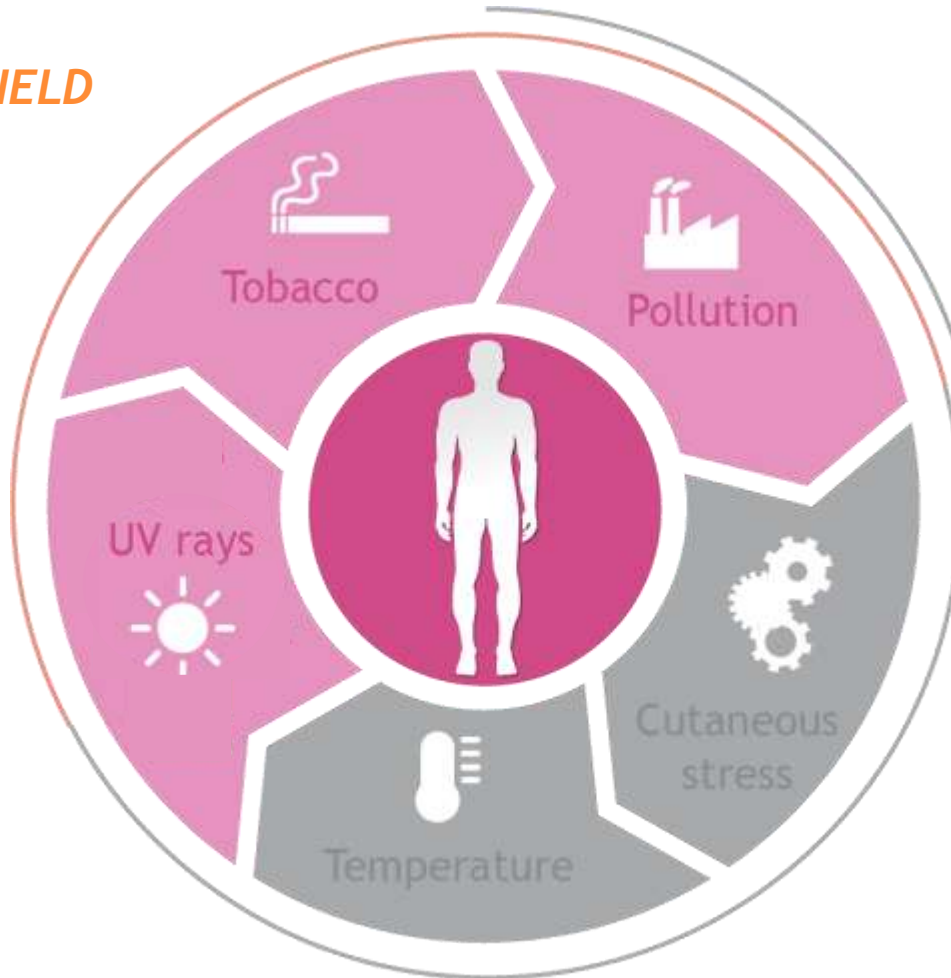
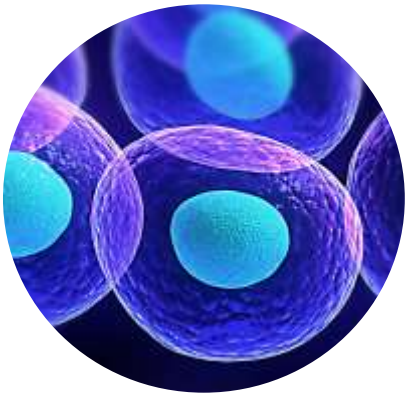
>> Osmo'city helps the removing of pollutants that would have asphyxiated the skin after a whole day in urban conditions

** significant $p < 0,01$

2. Biological shield : Cell'intact

2. BIOLOGICAL SHIELD

>> buckwheat seeds



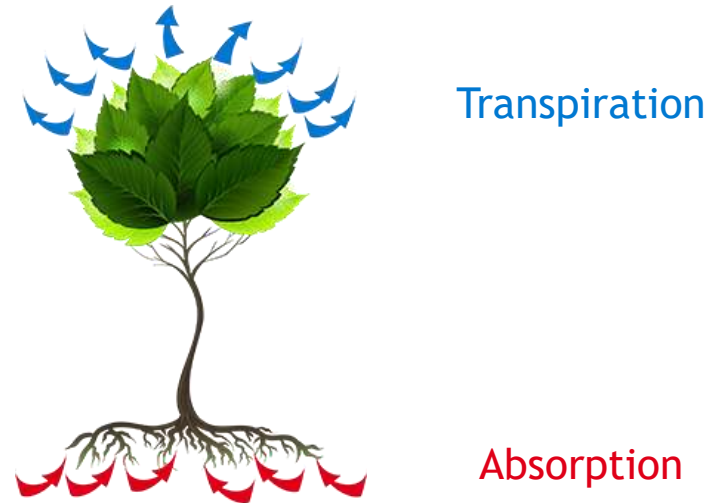
Buckwheat : Botanical aspect



- >> Polygonum Fagopyrum, Polygonaceae family
- >> Pseudocereal >> Gluten-free
- >> Traditionally consumed in France, Japan (soba)
- >> Crop traditionally used to regenerate soil
- >> Studied for heavy metal decontamination

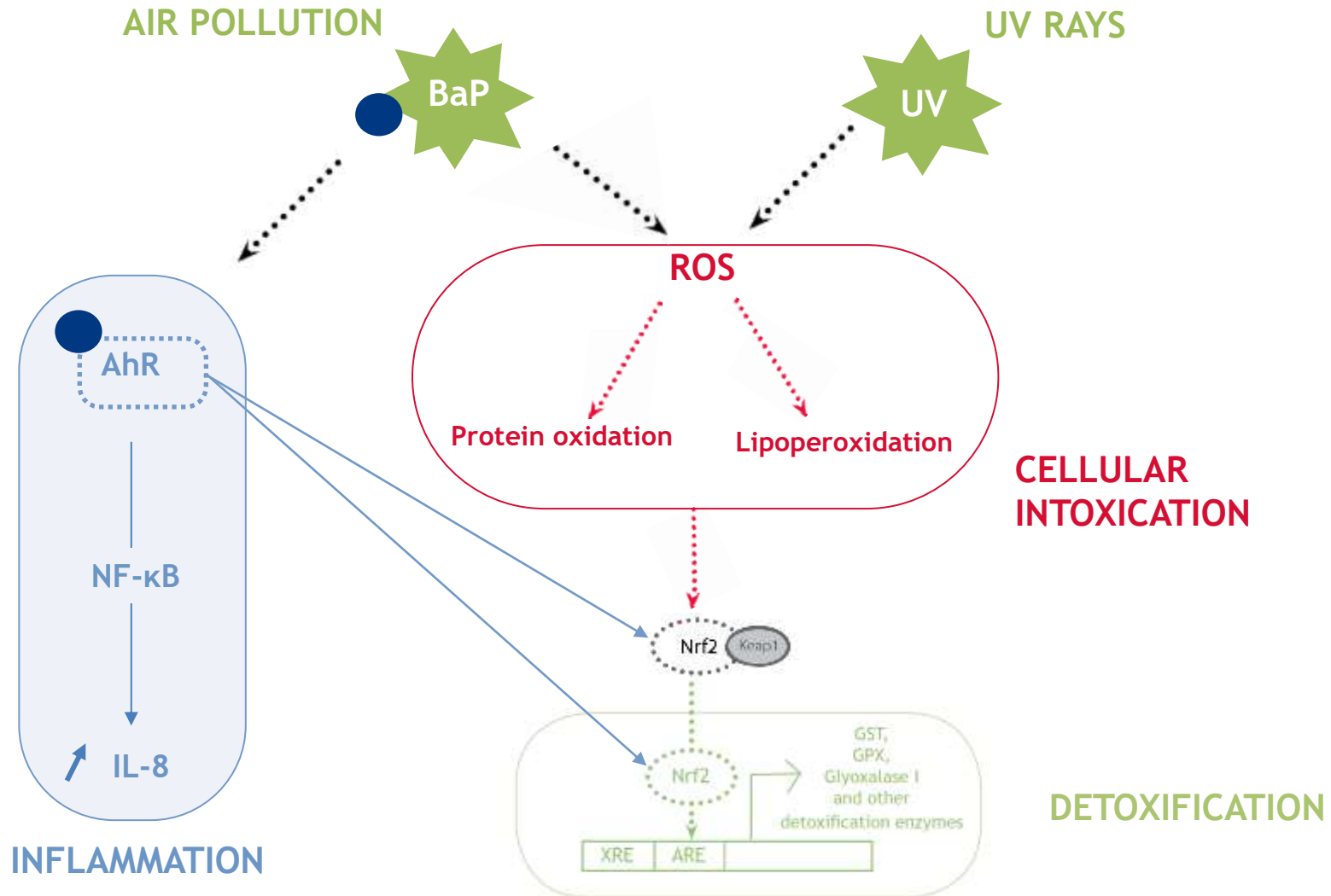
Buckwheat and phytoremediation

- >> Induces heavy metal uptake (zinc, copper) by transpiration (Tani FH et al.; 2006)

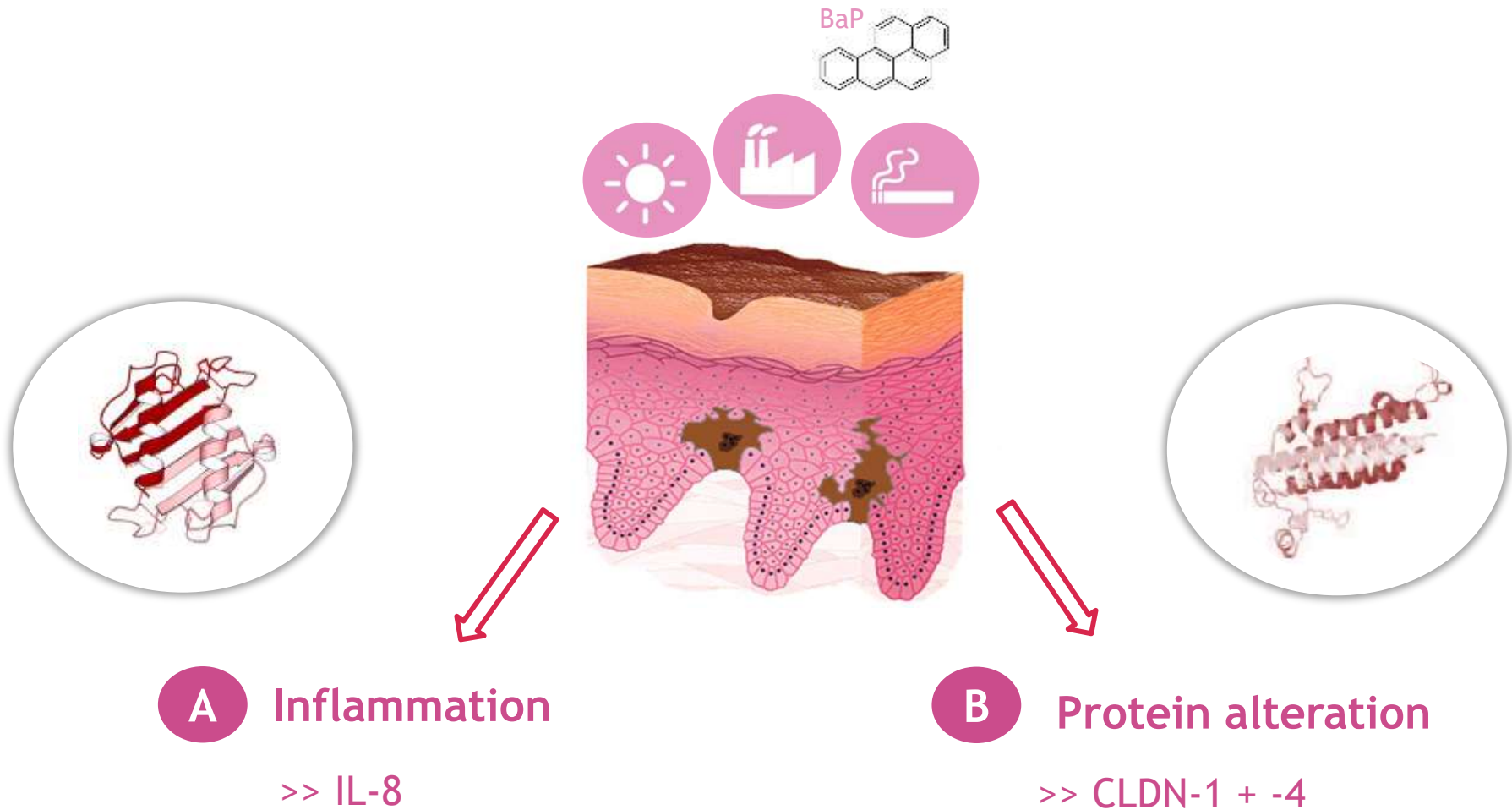


- >> Molecular mechanisms for external & internal detoxification (Yokosho K et al.; 2014)
- >> Aluminum detoxifying : identification of genes involved, (Yokosho K et al.; 2016)
- >> FeIREG1
- >> A natural source of cellular detoxification against environmental factors ?

Biological pathways

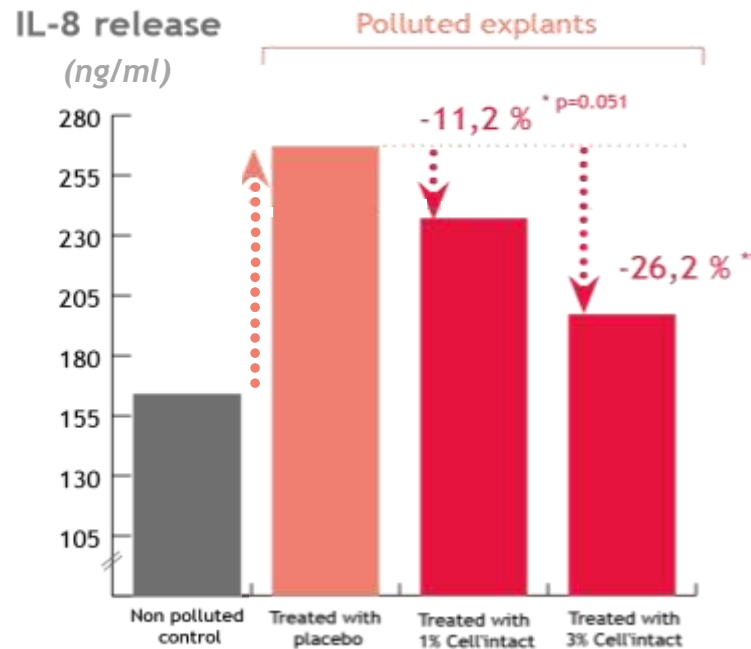


Two biological targets



Antipollution studies: results

A. Decrease in the proinflammatory response

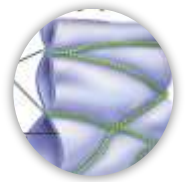


Significant (Student t-test ; $p < 0,05$) *: $0,01 < p < 0,05$ / **: $0,001 < p < 0,01$

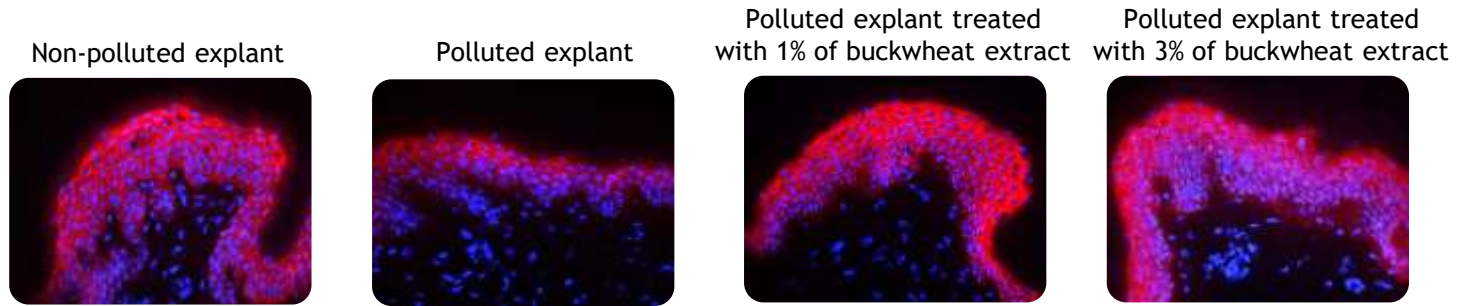
At 1 and 3% concentration, buckwheat extract significantly protects the skin from inflammatory stress induced by pollution

Antipollution studies: results

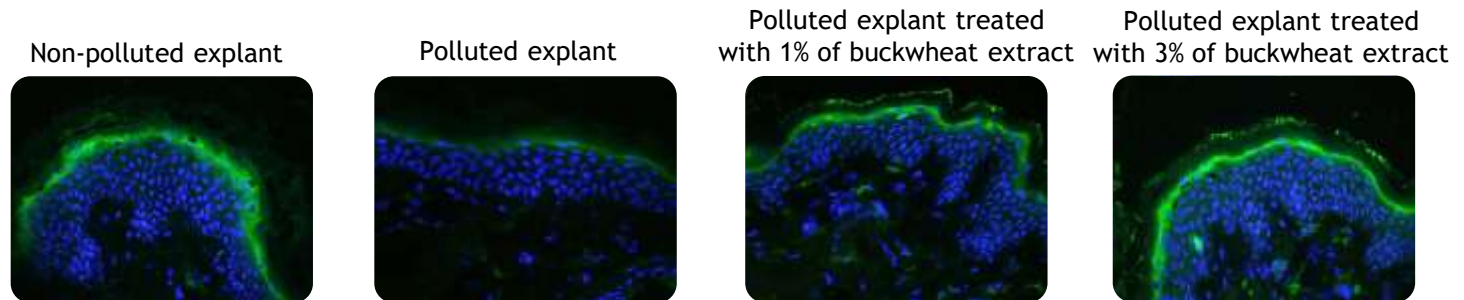
B. Protective action on tight junction proteins



Claudin-1

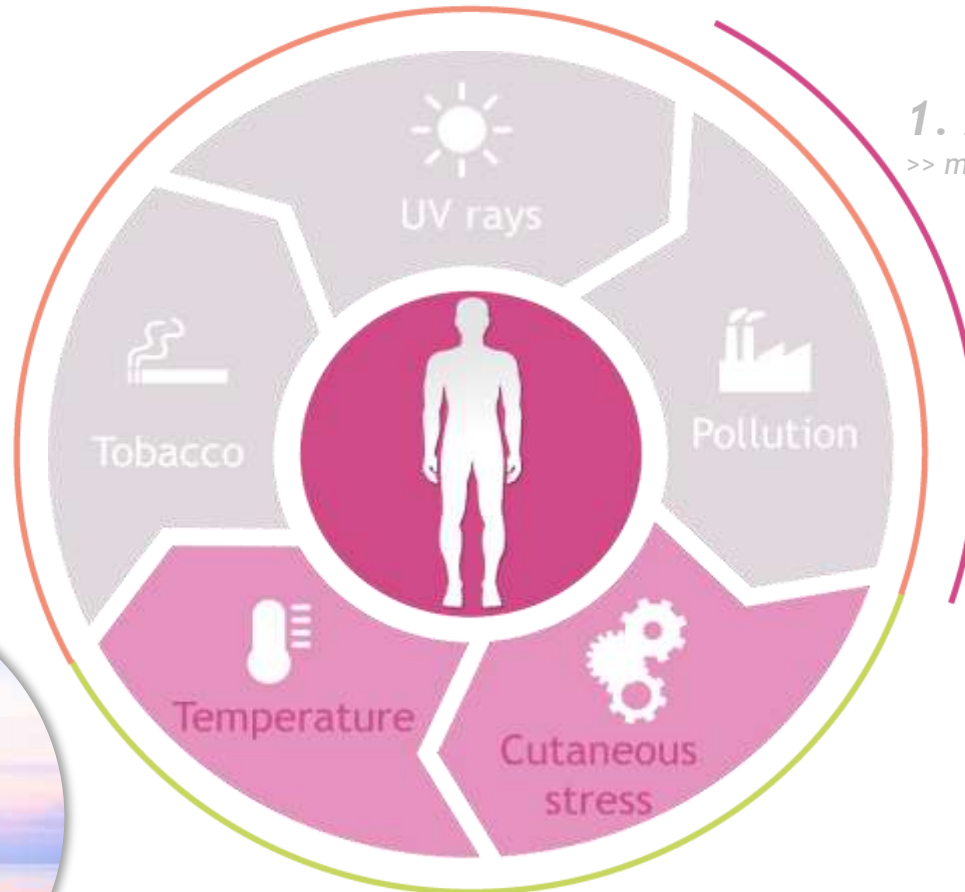


Claudin-4



Prevention of deterioration on CLDN1 and 4
Tissue integrity, homeostasis and epidermis barrier maintained
Protection from premature aging due to protein alteration

3. Soothing shield : Sens'flower



1. MECHANICAL SHIELD
>> marshmallow roots

3. SOOTHING SHIELD

>> saffron flower



A Co-Product Valorization Project



Focus on the Limousine chain



Experimental approach: 360° tests

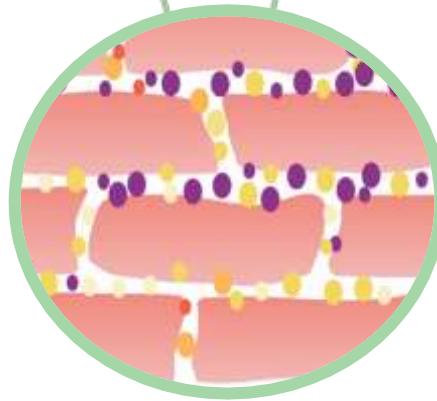
PROFILAGGRINE

Study of stimulation
of profilaggrin expression
(*in vitro*)

Skin barrier
function

LIPOPEROXIDATION

Study of β -carotene
protection (*in tubo*)



Experimental approach: 360° tests

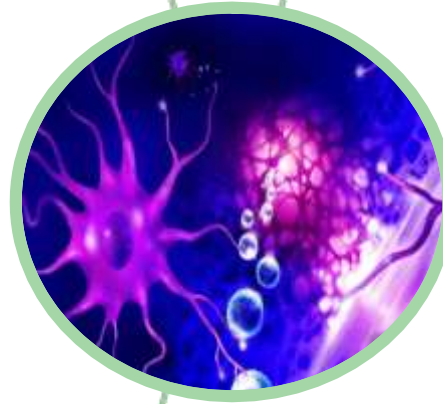
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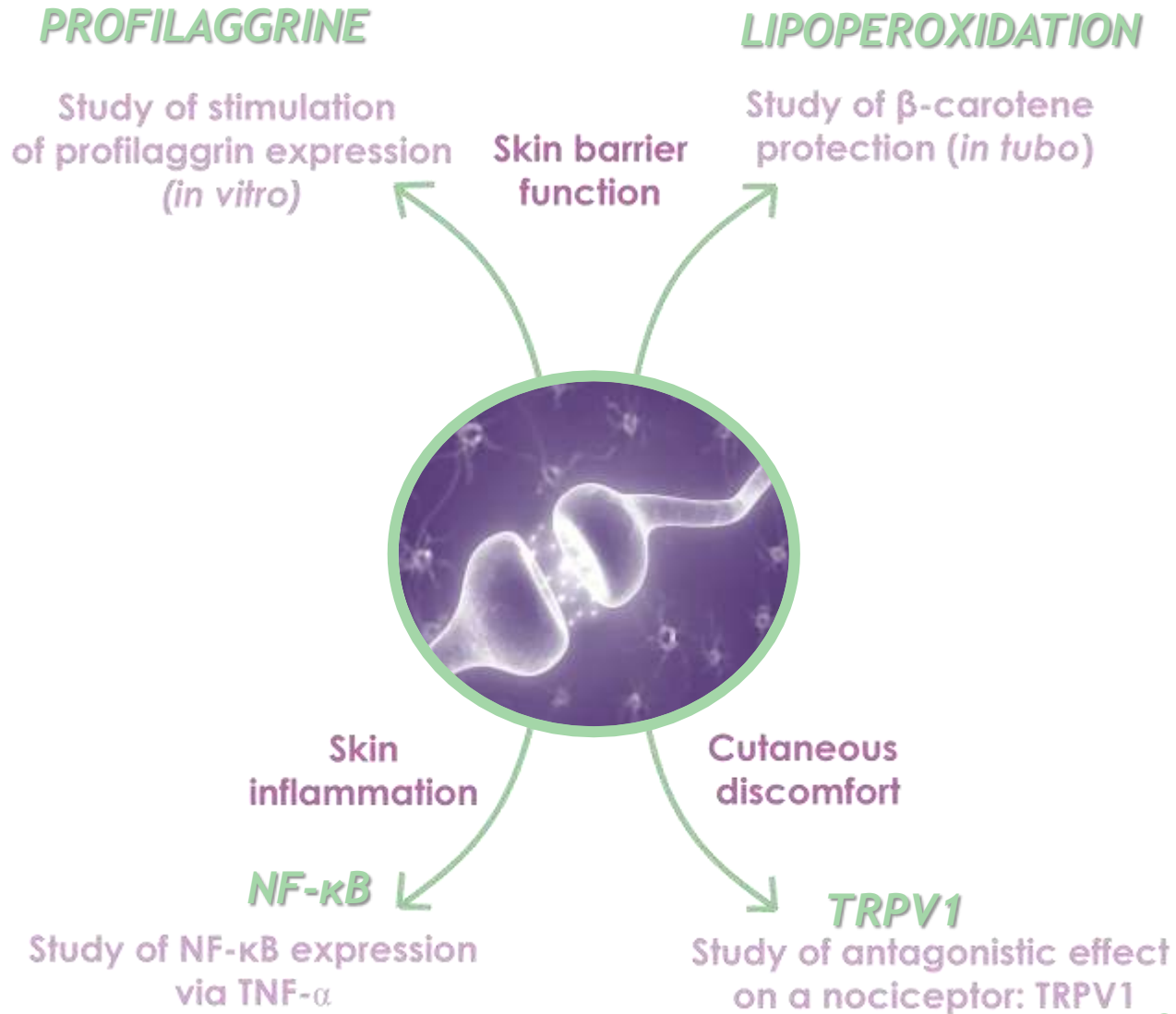


Skin
inflammation

NF- κ B

Study of NF- κ B expression
via TNF- α

Experimental approach: 360° tests

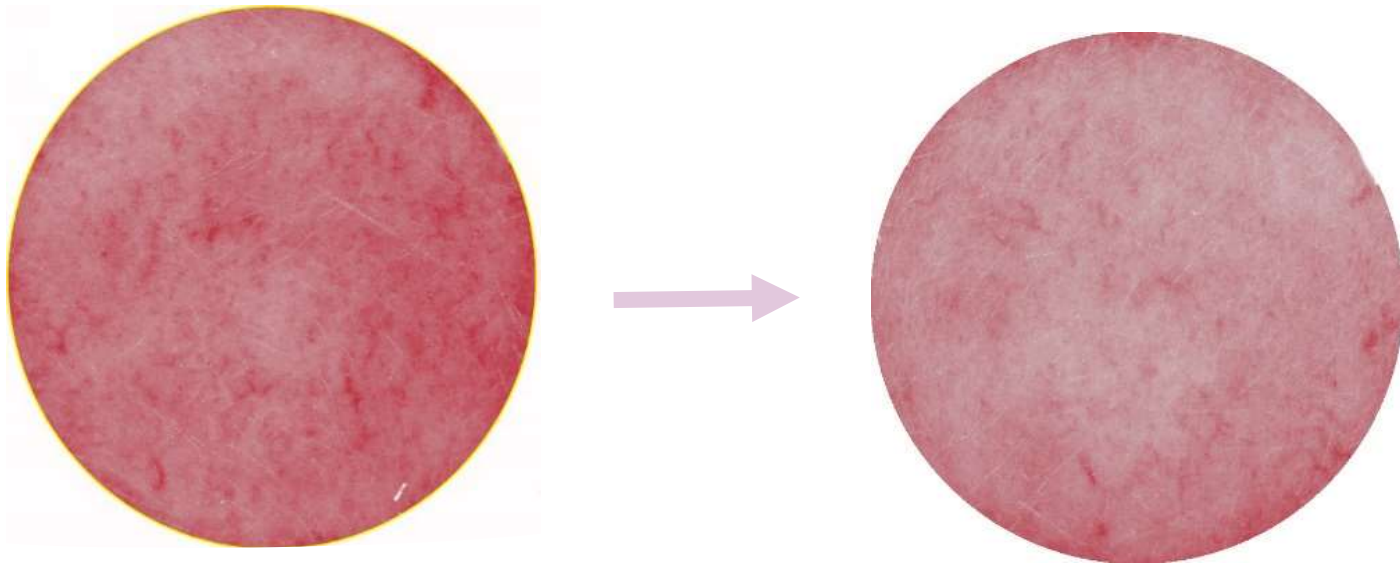


Sens'flower®: efficient on redness

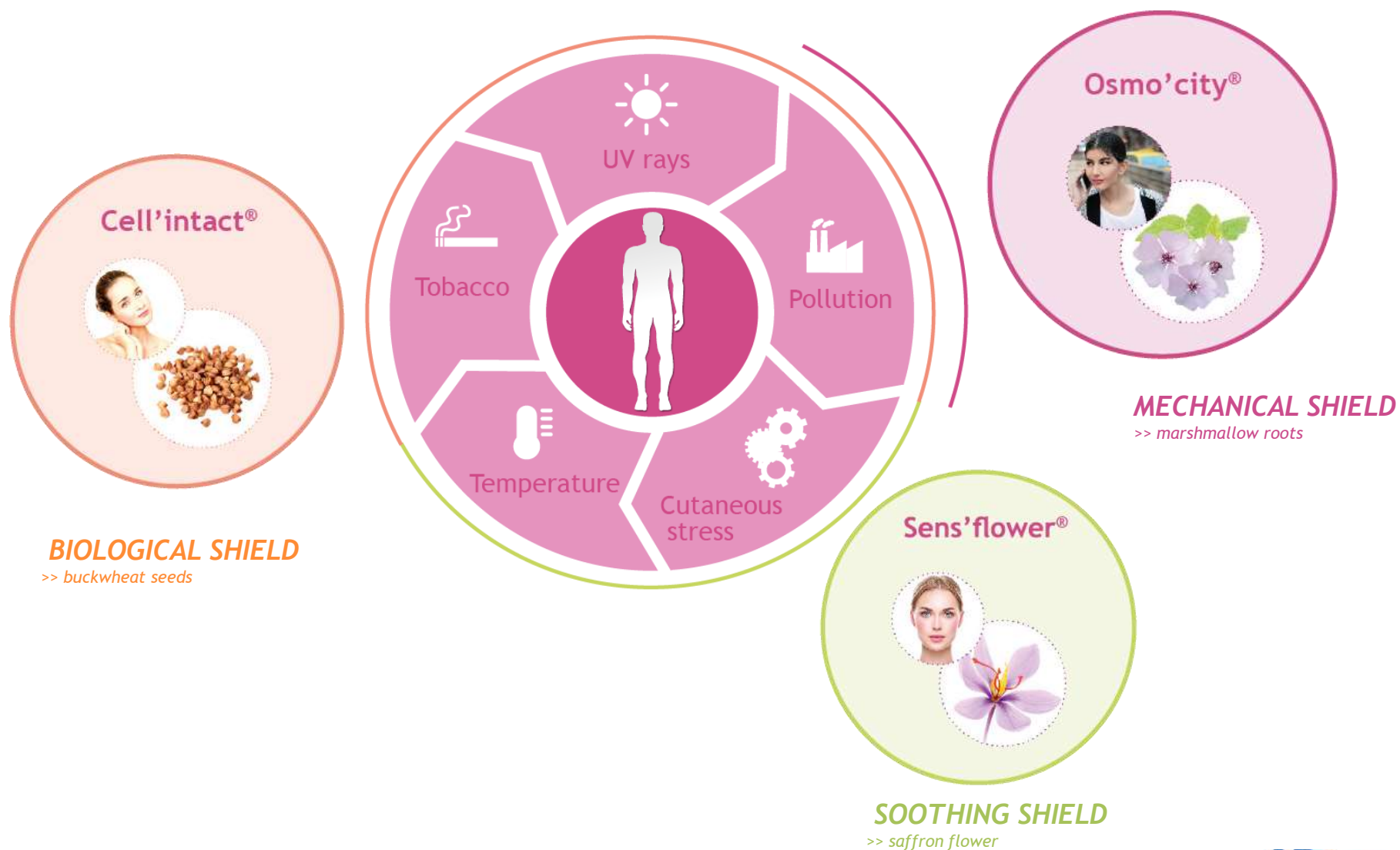


At 4% in formula allows up to a 16 % reduction in skin redness

>> Sens'flower® acts in efficiently reducing one of the visible signs of sensitive skin



Skin barriers and Exposome





adebiotech

13 & 14 Mars 2018

L'épigénétique dans la réponse du vivant
aux facteurs environnementaux

**Thanks for
listening**

ID bio
novacap group

