

# A fundamental discovery in aging: beyond the genome, the proteome



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 NAOS AGING SCIENCE

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état pur

# A change of paradigm for a new scientific era

# A SCIENTIFIC & HUMAN ENCOUNTER



Pr. Miroslav Radman

Jean-Noël Thorel



# Pr Miroslav RADMAN

## Geneticist & Biologist

Member of the Academy of Sciences in France & USA  
INSERM – CNRS  
Founder of MedILS (Mediterranean Institute  
for Life Sciences)

**40 YEARS OF RESEARCH  
STUDIES ON DNA REPAIR**



# 40 YEARS OF RESEARCH IN PROTEOME SCIENCE



Study of longevity  
heroes

EXTREMOPHILIC  
BACTERIA

- *Deinococcus radiodurans*
- when its DNA is damaged,
  - it is quickly fixed
  - by inoxidable
  - repairing proteins

# A SCIENTIFIC REVOLUTION

Longevity is not only linked to  
the genetic code

PROTEOME PROTECTION:  
key for cellular longevity



# NEW SCIENTIFIC PARADIGM



# THE PROTEOME

**PROTEINS =**

**1st main component after water**

**15 - 27.5% protein**

**STRUCTURAL**

**CELLS & TISSUES**

keratin, collagen, elastin...

**FUNCTIONAL**

**CELLULAR METABOLISM**

**& TISSUE HOMEOSTASIS**

enzymes, cytokines, hormones, growth factors...

Damages to the proteome are the

**ROOT CAUSE OF AGING**

# NEW SCIENTIFIC PARADIGM



PROTEOME  
PROTECTION

=

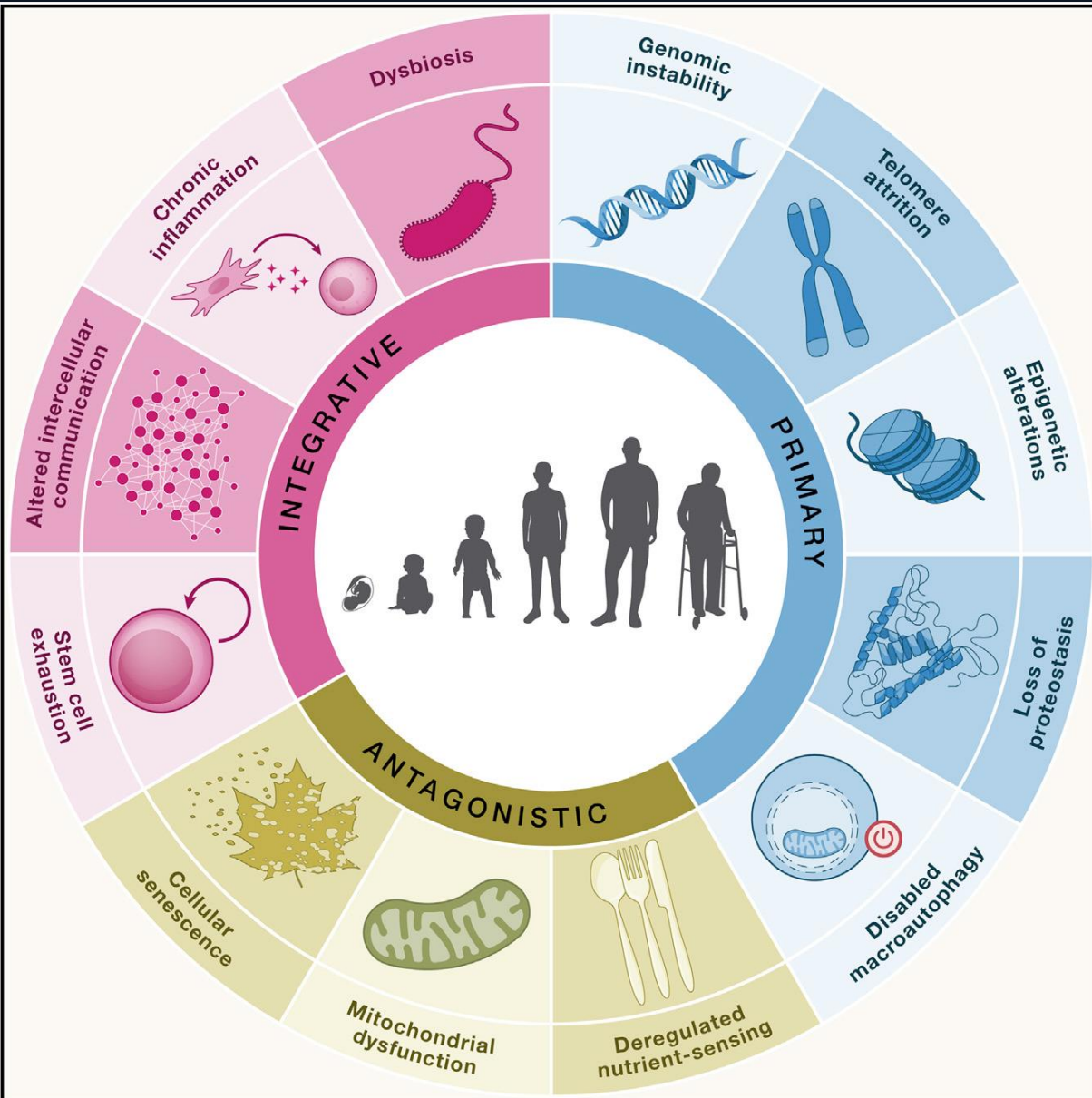
key for skin « longevity »  
= HEALTHY AGING

= « META THEORY »  
beyond most previous  
theories of aging



# META-THEORY of aging

12 hallmarks of aging



# META-THEORY of aging

Beyond the **GENOME**

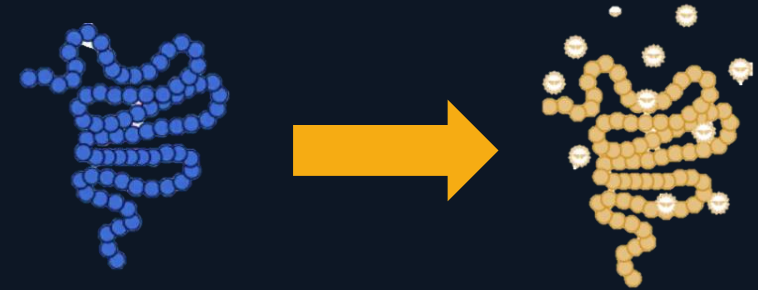
**The PROTEOME**



# ALTERATION of the PROTEOME, 1<sup>st</sup> cause of aging

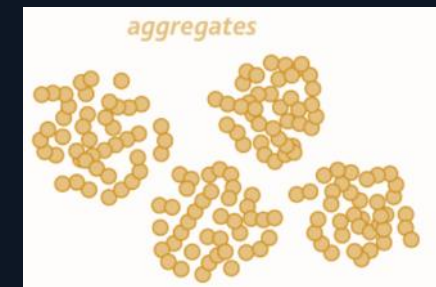
## CARBONYLATION

Freezes proteins, leading to their inactivation.



CARBONYLATED PROTEINS

- Irreversible reaction
- Formation of toxic aggregates that hinder cellular physiology
- Acceleration of aging



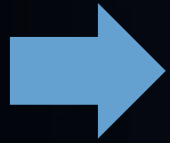
AGGREGATES

# CONSEQUENCES ON THE SKIN

- Carbonylation of surface proteins
- Carbonylation of extracellular matrix proteins

↘ RADIANCE

↘ EVENNESS

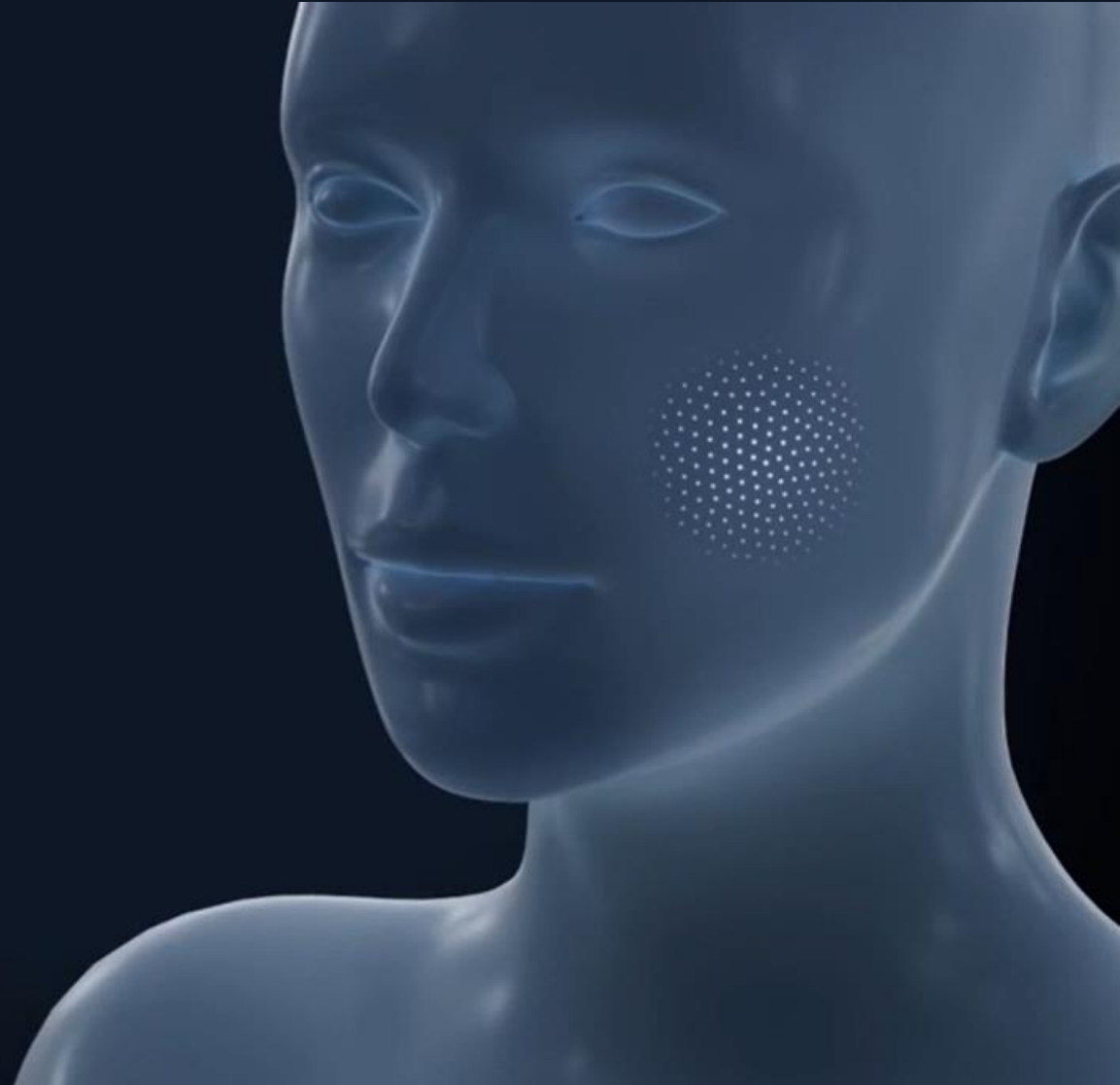


↗ WRINKLES

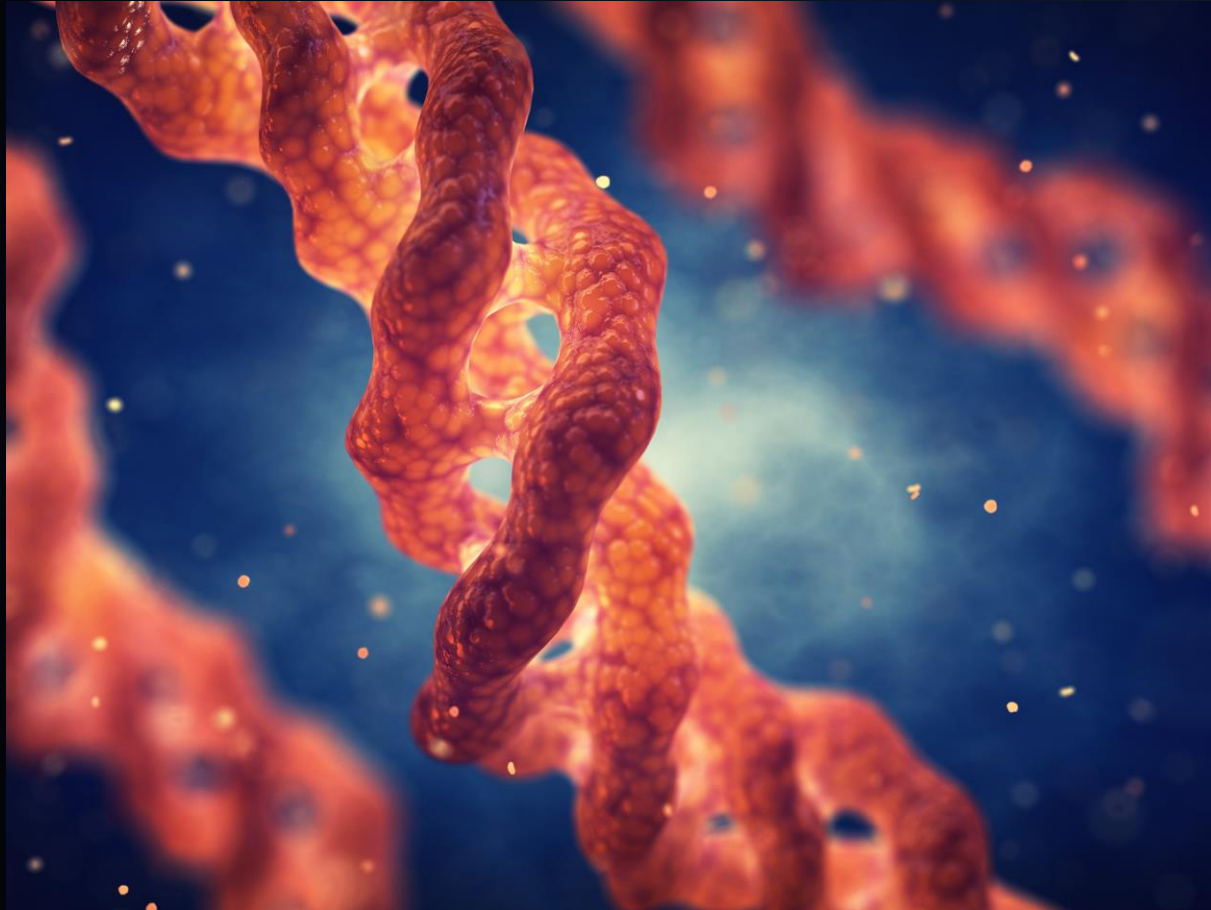
↘ FIRMNESS

↘ DENSITY

Impact on the 5 main signs of skin aging



# FUNDAMENTAL STRATEGY TO PREVENT PREMATURE AGING



## PROTECT THE PROTEOME

HOW ?

Two-pronged mechanism of action:

- Chaperone molecules, physical mechanism: stabilize the conformation of proteins
- Antioxidant molecules, biological mechanism: neutralize the carbonylation inducers

**ANTIOXYDANT CHAPERONES**

NAOS AGING SCIENCE  
Ecobiology-driven R&D Strategy

***Arthobacter agilis***  
**Snow bacteria**

Extremophilic bacteria  
ultra-resistant to:

**UV**

**COLD**

**OXYDATIVE STRESS**



micro-organism capable of  
self-repair & survival in  
extreme conditions

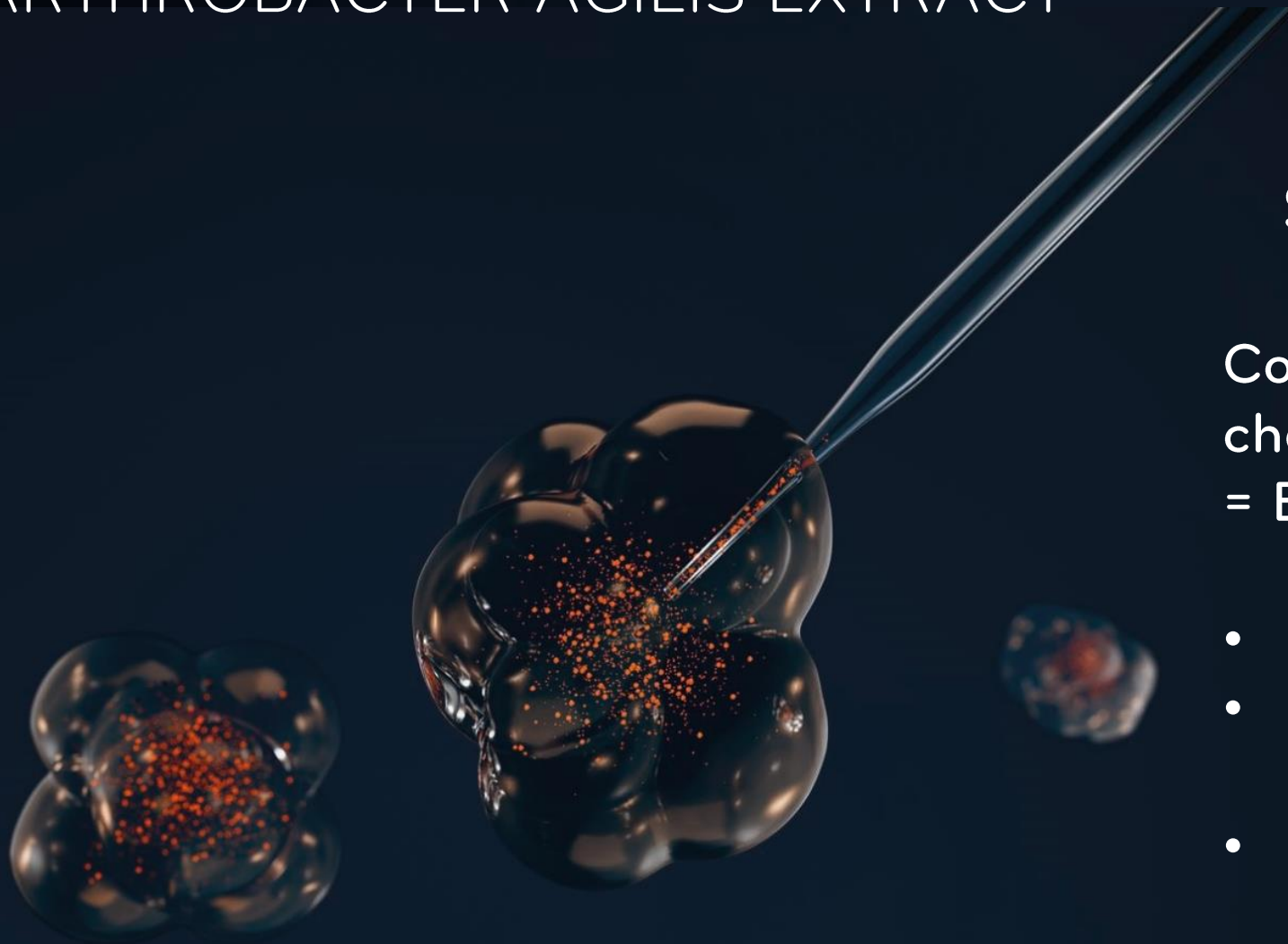
# AGE PROTEOM™ PATENTED BIOTECHNOLOGY ARTHROBACTER AGILIS EXTRACT

## SNOW BACTERIA

Combination of 6 antioxidant  
chaperones  
= BACTERIORUBERINS

- Unique form in nature
- Special affinity for proteins -> protective chaperone activity
- Powerful antioxidant

*3,8 billion years of evolution*



# AGE PROTEOM™ PATENTED BIOTECHNOLOGY

## CHAPERONE-LIKE ACTIVITY

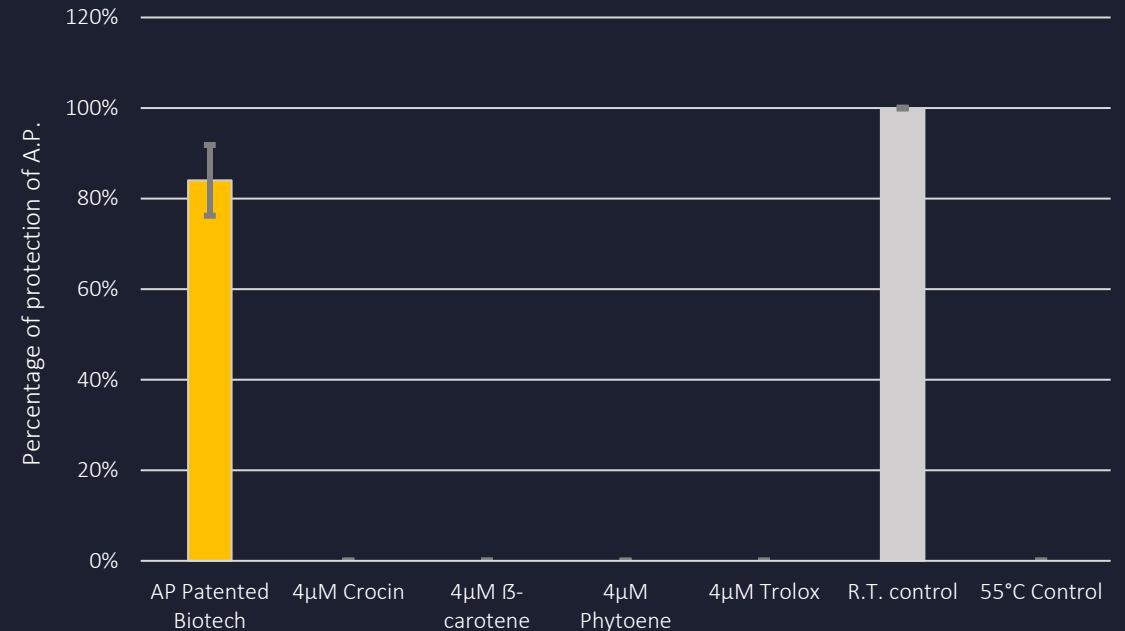
*in tubo*

Among all the molecules tested, only AGE PROTEOM™ patented biotechnology shows a protein chaperone effect

>80% protection

Stabilization of 3D structure

**Specific 'chaperone effect' - Heat test**  
uses heat to destabilize protein alkaline phosphatase



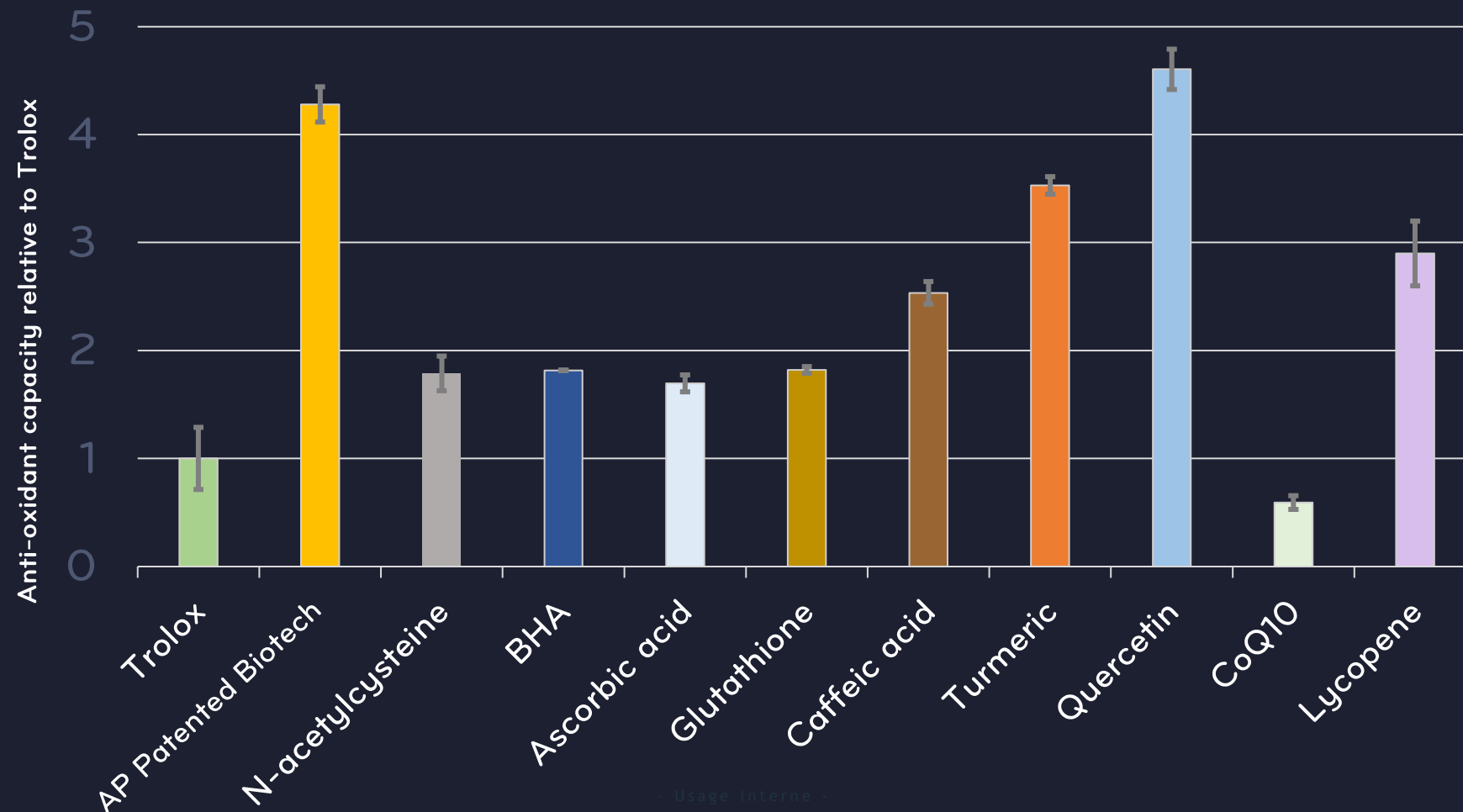


# AGE PROTEOM™ PATENTED BIOTECHNOLOGY

## ANTIOXYDANT POWER

*in tubo*

**AGE PROTEOM™ patented biotechnology shows a strong antioxidant potential, higher than reference antioxidant molecules**

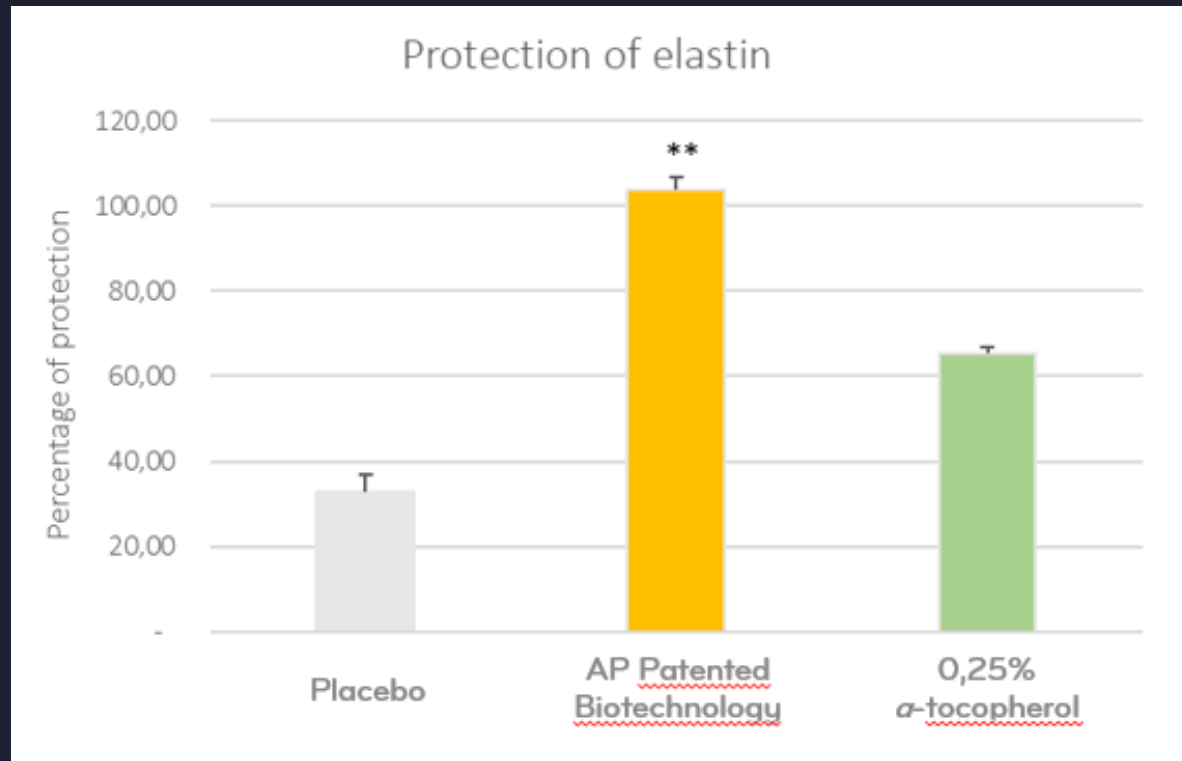


# AGE PROTEOM™ PATENTED BIOTECHNOLOGY

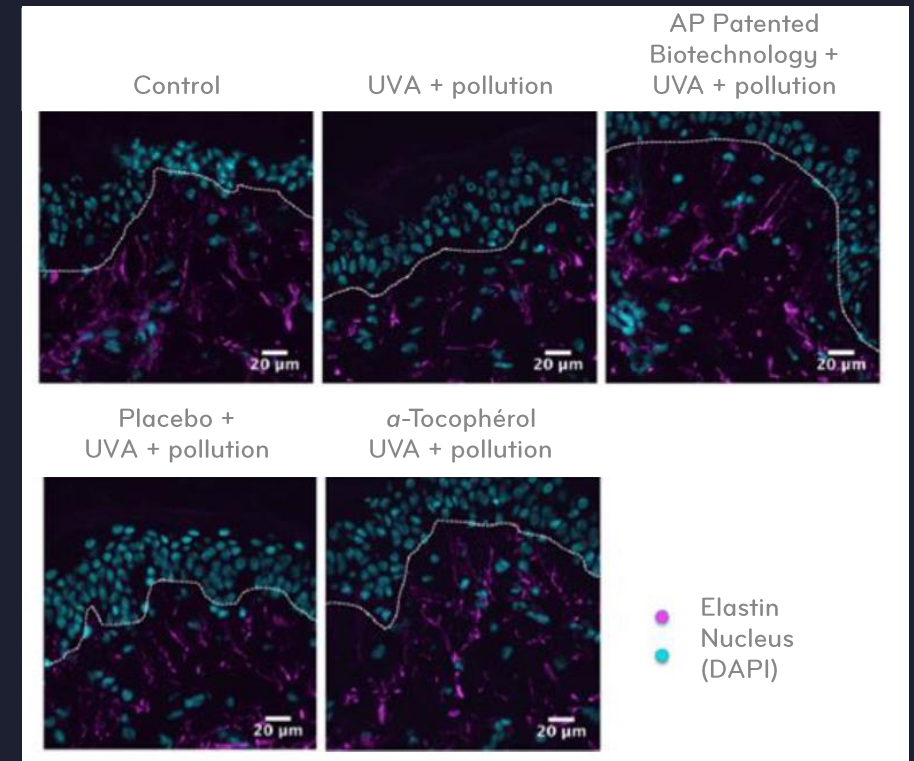
## STRUCTURAL PROTEINS PROTECTION

*ex vivo*

AGE PROTEOM™ patented  
biotechnology protects elastin from  
OXIDATIVE STRESS



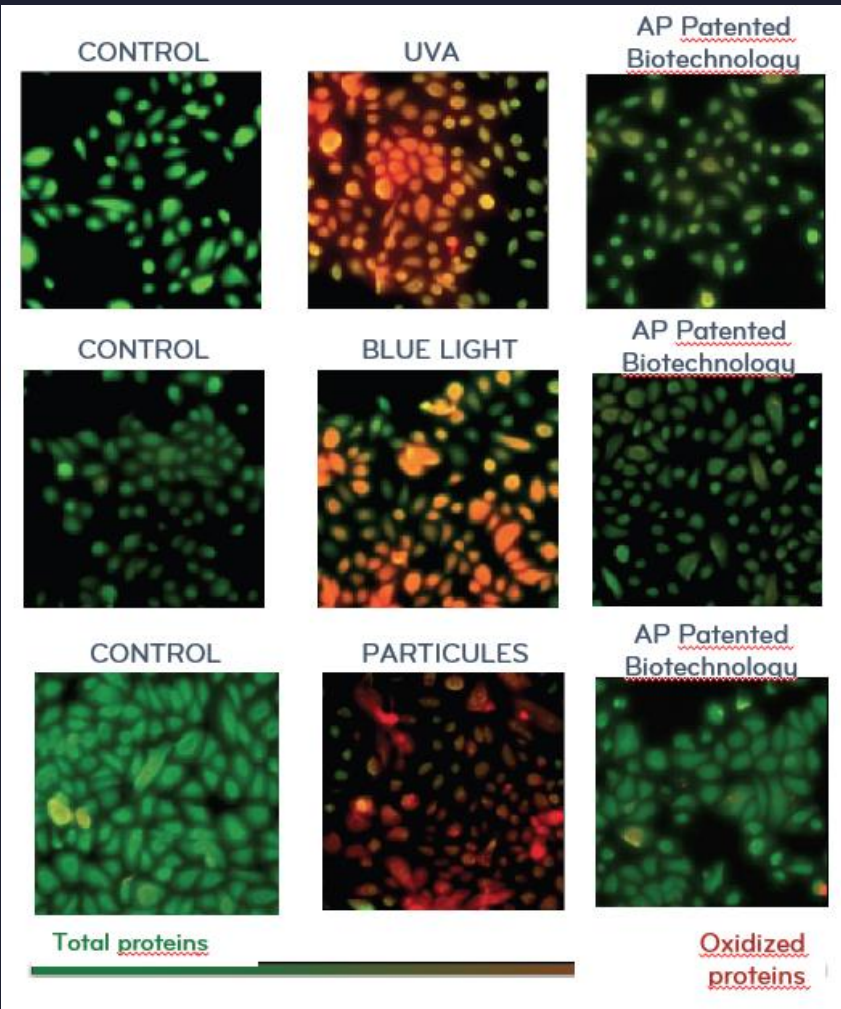
Skin explants  
UVA & POLLUTION STRESS



# AGE PROTEOM™ PATENTED BIOTECHNOLOGY

## PROTECTION AGAINST CARBOXYLATION

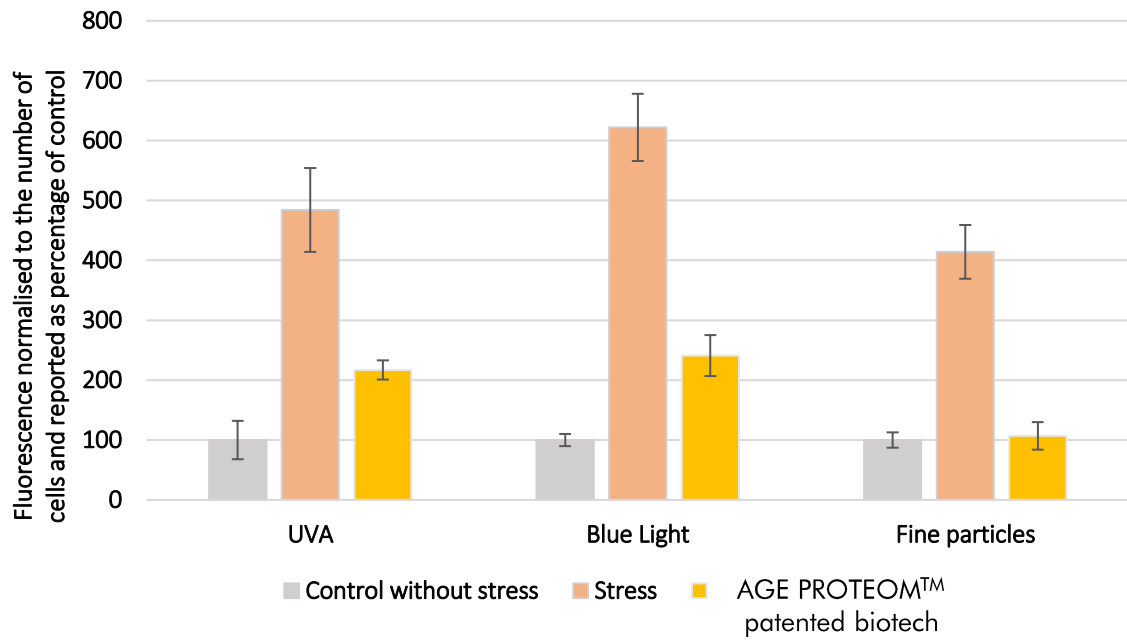
*In vitro*



# AGE PROTEOM™ patented biotechnology

protects proteins from carbonylation induced by various environmental factors

## UV, BLUE LIGHT and POLLUTION



*Cultured keratinocytes exposed to different stresses  
Imaging and quantification of protein carbonyls*

# AGE PROTEOM™ PATENTED BIOTECHNOLOGY

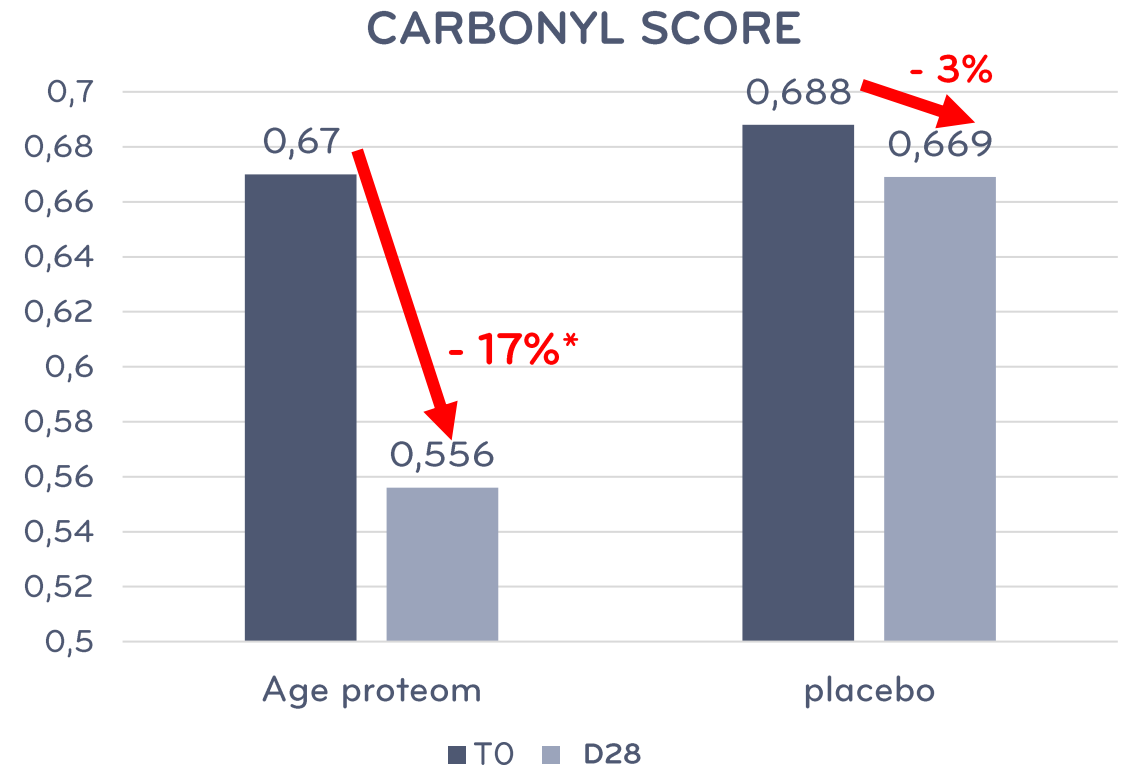
## PROTECTION AGAINST CARBONYLATION

*in vivo*

Helps reduce the level of protein carbonylation compared to placebo.

### 28 DAYS CLINICAL TRIAL

23 women, 38 to 69 yo, phototypes II to III, smokers and with a dull complexion  
Twice daily application – hemi-face



\* Significant (Student t test)

# A NEW SCIENTIFIC ERA: PROTEOME PROTECTION



## WHAT?

Proteome-centric versus DNA-centric  
R&D strategy

## WHY?

Proteome protection = "META  
THEORY" beyond all theories of aging

## HOW?

Chaperone antioxidants  
versus « regular » antioxidants



Thank you for your attention



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