NAOS AGING SCIENCE

BIODERMA LABORATOIRE DERMATOLOGIQUE · INSTITUT ESTHEDERM PARIS · état pur

TOWARDS A META-THEORY OF SKIN AGING

THE PROTEOME PARADIGM

Exclusive research partnership

NAOS AGING SCIENCE

Prof. Radman
MedILS (Mediterranean Institute for Life Sciences)

AN INTERNATIONAL SCIENTIFIC PARTNERSHIP

NAOS AGING SCIENCE & Pr. RADMAN

Prof. Miroslav RADMAN
FUNDAMENTAL RESEARCH ON LONGEVITY AND CELL REGENERATION

A major discovery in the understanding of aging and age-related pathologies:
Parkinson's, Alzheimer's, Charcot, diabetes...

Founder of MEDILS

Geneticist, specialist in skin aging
Member of the French & USA Academy of Sciences
Founder of MedILS *(Mediterranean Institute for Life Sciences)*

A SHARED VISION OF THE SKIN AND AGE

Since the 2000s, Jean-Noël Thorel, pharmacist and founder of NAOS, has shared the vision and research of Professor Miroslav Radman, whose work on cell longevity and regeneration has revolutionized the understanding of aging and age-related pathologies. The scientific research partnership enabled NAOS' research teams to work on the cutaneous application of the scientist's results. The skin's biological age is not necessarily related to the individual's chronological age: if we protect and optimize the biological robustness of our proteins, and consequently of our cell repair systems, the entire functionality of youth is preserved. The partnership between NAOS AGING SCIENCE and MedILS has made it possible to implement this powerful and revolutionary scientific approach. **BIODERMA**'s dermatological expertise and the cosmetic know-how developed by **Institut Esthederm** for over 40 years have been combined to develop one of the most promising biological pathways: **protecting the proteome as a response to skin aging.**

WHY TARGET THE PROTEOME RATHER THAN THE GENOME?

While genes constantly carry all biological information *(= what could happen)*, not all our genes are expressed everywhere in our body at all times. It is only when a gene is translated into a protein that it is fully expressed *(= what really happens)*. **The proteome is a dynamic entity that constantly adapts to the needs of the cell and its environment[1]. It is therefore the starting point of all the vital functions of the skin. Its alteration is the main cause of aging.**

THE CUTANEOUS PROTEOM
= ALL SKIN PROTEINS

PROTEINS

PROTEINS ARE THE 2nd CONSTITUENT *of the skin after water*

STRUCTURAL ROLE framework & FUNCTIONAL ROLE *ensure the proper functioning of all physiological processes*

A NEW UNDERSTANDING OF AGING:
THE PROTEOM, RESPONSIBLE FOR LONGEVITY

In the same way as in the organism, the thousands of proteins essential to the skin's physiology play a structural as well as functional role. They constitute the fabric, frame and density of skin layers, like **elastin or collagen**. They also make sure that all vital physiological processes such as breathing, **repair, communication** and cell waste **disposal** work properly. These proteins, which are essential to cell life, are limitless: DNA repair enzymes, **hormones, connexins**, which mediate cell communication, **aquaporins**, which carry water through various epidermal layers… all these roles are performed by multiple specialized proteins that ensure the health and balance of our largest organ: the skin.

PROTECTING THE INTEGRITY OF THE PROTEOME IN THE LONG TERM HELPS PRESERVE THE SKIN'S YOUTHFULNESS

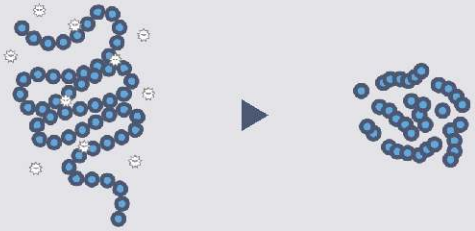
BIBLIOGRAPHY *(1) Radman M. Ecobiological approach to research regarding ageing and diseases. European Journal of Dermatology 2019 29:1. 2019;29(1):11-14. doi :10.1684/EJD.2019.3534*

CARBONYLATION OF PROTEINS

THE MOST SERIOUS CELL & TISSUE OXIDATION

1ST CAUSE OF PREMATURE SKIN AGING

CARBONYLATED PROTEIN **AGGREGATES**

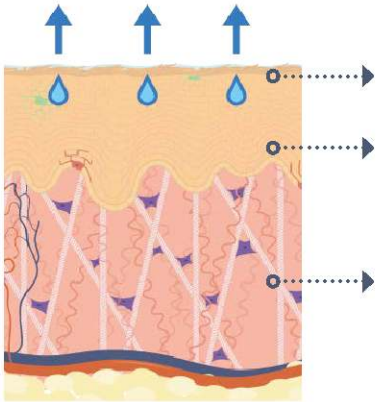


LOSS OF STRUCTURE & FUNCTION
With age, carbonylated proteins accumulate in toxic aggregates [2]. Leading to ***premature aging.***

THE AGING CHEMISTRY OF ANY CELL, INCLUDING SKIN CELLS, INVOLVES THE OXIDATION OF PROTEINS.

With time and harsh external factors, skin proteins are subject to various alterations, the biggest threat being carbonylation, an irreversible phenomenon linked to oxidation. Carbonylated proteins can no longer perform their biological functions, which is why they must be recycled or eliminated.

With age, they are more difficult to eliminate and accumulate in the form of toxic aggregates which hinder cell physiology. These **protein aggregates are both aging markers and accelerators**. By clogging up cell detoxification systems, they transform proteostasis, essential to balanced life, into proteotoxicity, which accelerates aging.



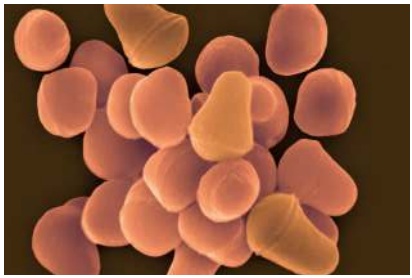
STRATUM CORNEUM
Increased transepidermal water loss [3]
▶ **DEHYDRATATION**

EPIDERMIS
Increased keratin carbonylation [4]
▶ **ALTERATION OF BRIGHTNESS**
▶ **LOSS OF COMPLEXION HOMOGENEITY**

DERMIS
Fibroblasts morphological changes & dermal proteins production changes [5]
▶ **DERMAL MATRIX ALTERATION**
▶ **LOSS OF DENSITY, LOSS OF FIRMNESS, WRINKLES**

(2) Dalle-Donne I, Giustarini D, Colombo R, Rossi R, Milzani A. Protein carbonylation in human diseases. Trends in Molecular Medicine. 2003;9(4):169-176. doi:10.1016/S1471-4914(03)00031-5
(3) Iwai I, Hirao T. Protein carbonyls damage the water-holding capacity of the stratum corneum. Skin pharmacology and physiology. 2008;21(5):269-273. doi:10.1159/000148042
(4) Iwai I, Ikuta K, Murayama K, Hirao T. Change in optical properties of stratum corneum induced by protein carbonylation in vitro. International Journal of Cosmetic Science. 2008;30(1):41-46. doi:10.1111/j.1468-2494.2008.00426.x (5) Yamawaki Y, Mizutani T, Okano Y, Masaki H. The impact of carbonylated proteins on the skin and potential agents to block their effects. Experimental dermatology. 2019;28 Suppl 1:32-37. doi:10.1111/EXD.13821

NAOS ADVANCED RESEARCH DISCOVERY



THE LONGEVITY MOLECULE

Exploiting the extremes : Arthrobacter agilis, a bacterium with unique properties

Some molecules of this bacterium have a physical shield function similar to that of natural chaperones, combined with powerful antioxidant properties.

The *Arthrobacter agilis* bacterium, has an amazing ability to survive, which allows it to withstand the most extreme temperatures, UV rays and oxidative stress.

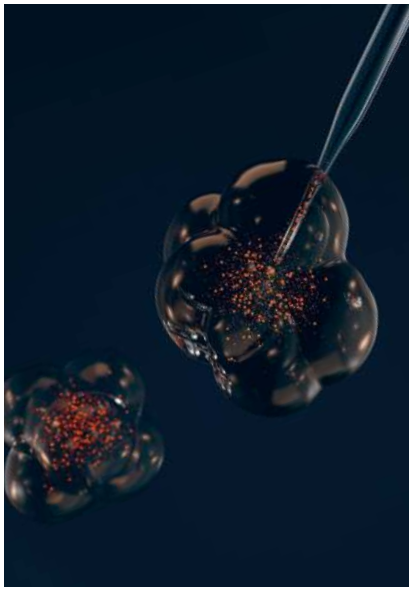
Its ability to survive in extreme conditions is thanks to the presence of 6 bacterioruberins that are powerful antioxidants with a chaperone effect, capable of durably protecting its proteome. The NAOS applied research laboratories managed to extract these bacterioruberins to create the Age Proteom™ patented biotechnology.

WHEN ITS DNA IS DAMAGED, IT IS IMMEDIATELY REPAIRED BY PROTEINS

ITS PROTEOME RESISTANCE IS KEY TO LONGEVITY ENSURED BY SPECIFIC ANTIOXIDANT CHAPERONES.

AGE PROTEOM™ PATENTED BIOTECHNOLOGY

PROTECTION OF THE PROTEOM WITH MIMETIC INSPIRED ANTIOXIDANT CHAPERONES



THE KEY OF CELL LONGEVITY

Inspired by Prof. Radman's work and developed by NAOS AGING SCIENCE.

AGE PROTEOM™ PATENTED BIOTECHNOLOGY

Targeting the cause of skin aging, to optimize cell longevity, Age Proteom™ patented biotechnology is the first antioxidant chaperone ever described.

As a result of the NAOS ecobiological approach, bacterioruberins from Arthrobacter agilis have demonstrated a strong affinity with skin proteins and a unique "chaperone-like antioxidant" activity.

They are capable of protecting the skin proteome to tackle aging at source :

- *Protection of structural proteins: elastin*
- *Protection of functional proteins: DNA repair*
- *Protection against harsh environmental factors: UV, blue light, pollution*
- *Protection against carbonylation, irreversible damage to proteins*

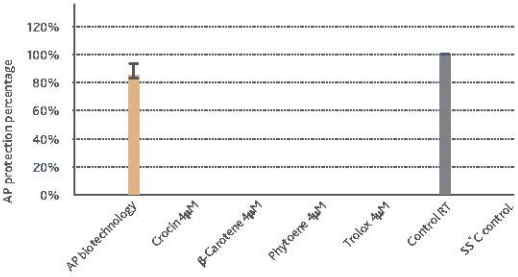
PATENTED BIOTECHNOLOGY :

1ST PROTEOME PROTECTION ACTIVE INGREDIENT WITH AN *"ANTIOXIDANT CHAPERONE"* MECHANISM

1 Protein protection CHAPERONE-LIKE ACTIVITY *(physical shield)*

With more than 80 % protective efficacy, this active ingredient creates a genuine physical shield that preserves the structure of proteins, allowing them to remain functional over the long term.

CHAPERONE EFFICACY - SPECIFIC PROTECTION OF PROTEINS
Chaperone effect of various molecules

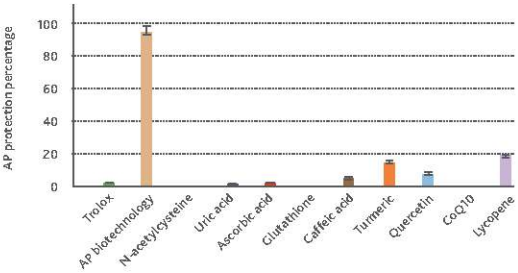


AP-Heat test / uses heat to destabilize the alkaline phosphatase protein (AP) (specific chaperone effect test).

2 Protein protection ANTIOXIDANT ACTIVITY *(biochemical shield)*

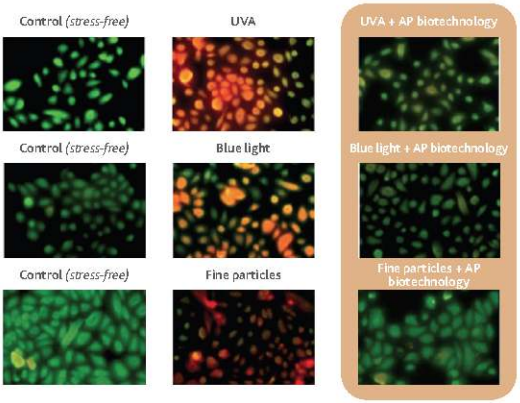
Its protein protective power is largely superior to that of reference antioxidant molecules *(CoQ10, glutathione, ascorbic acid, lycopene).*

SUPERIOR ANTIOXIDANT EFFICIENCY TO REFERENCE ANTIOXIDANTS
Protein protective power



APox test / uses the activity of alkaline phosphatase (AP) as a marker of protein protection against oxidative stress. The more significant AP activity is, the higher the protection against free radicals.

In vitro TEST: PROTECTION OF SKIN PROTEINS AGAINST CARBONYLATION CAUSED BY UVA RAYS, BLUE LIGHT AND PARTICULATE POLLUTION



In vitro test on normal human epidermal keratinocytes (NHEK) cultured before being brought into contact (or not) with the active ingredient, and then subjected to stresses (UVA, blue light or fine particles).

The Age Proteom™ patented biotechnology protects keratinocytes against all major harsh environmental factors.

STRESS	PROTECTION FACTOR
UVA	63.8%
Blue light	73%
Fine particles	96.2%