

CELL 2 CELL REPAIR CLINICAL STUDIES



NEUROGUARD – Pioneering Neurocosmetic Anti-age solution

Neuroguard opens the door to new neurocosmetic strategies. Beyond nervecell communications, it decrypts, targets and provides preventive and curative treatment against skin neuroaging. Our laboratories have indeed demonstrated that the aging of neurons directly affects the communication between nerves and fibroblasts, triggering a fall in fibroblasts vitality and a decrease in collagen and elastin synthesis. Neuroaging promotes Fibroaging.

FIGHTING AGAINST SKIN NEUROAGING

To reestablish a healthy communication between nerves and fibroblasts and to reactivate dermal cells previously weakened by neuroaging toxicity. Fighting against neuroaging enables delaying fibroaging. Thanks to the reactivation of collagen and elastin synthesis, Neuroguard treats deep wrinkles within 28 days.

ARE NEURONS SUBMITTED TO AGING?

Medical searches have demonstrated that nerves are subjected to aging as other cellular types; this process is called neurodegeneration. The study of the neurodegeneration process has highlighted the major role of a neurotoxic peptide called amyloid beta (Ab), which forms senile plaques on the surface of nerve endings.

WHO IS AB?

This neurotoxic peptide comes from a membrane protein known as Amyloid Precursor Protein (APP), which is located on the neuron surface. As its name implies, this protein is a precursor that can be cleaved in two different ways. First type of cleavage is triggered by a secretase enzyme and gives rise to the liberation of neurotoxic A. The second type of cleavage is triggered by a secretase enzyme and gives rise to the liberation of a sAPP peptide, which, contrary to A, has neuroprotective properties.

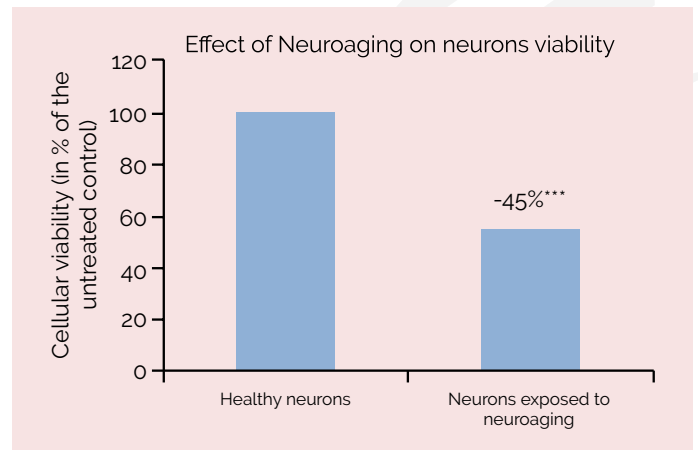
These two cleavages exist in a balanced manner within a neuronal population that could be qualified as young. Aging, and in general the accumulation of oxidizing stress, leads to a gradual imbalance, where the cleavage liberating the neurotoxin becomes dominant, triggering the neuronal degeneration process that we call neuroaging.

WHAT IS THE IMPACT OF NEUROAGING ON SKIN PHYSIOLOGY?

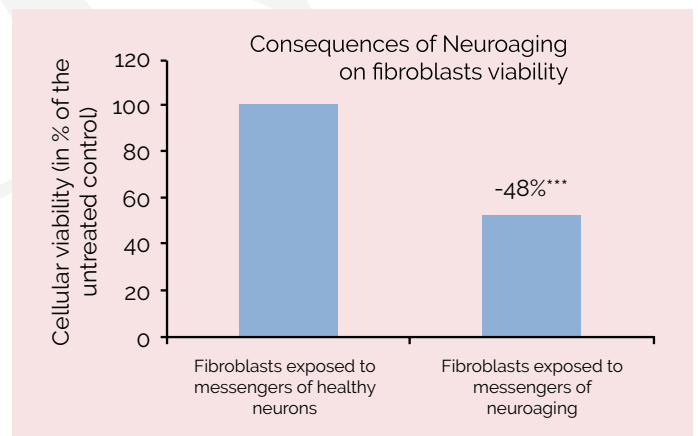
In the skin, nerves continuously communicate with other cutaneous cells through neurotransmitters.

STUDY OF NEUROAGING PROCESS AND ITS CONSEQUENCES ON FIBROBLASTS ACTIVITY

The hypothesis tested is whether neurons placed under Neuroaging conditions secrete messengers that are potentially toxic for fibroblasts. In the following studies, Neuroaging is simulated by the addition of the Ab factor ($1\mu\text{M}$) to cultures of embryo cortical neurons.



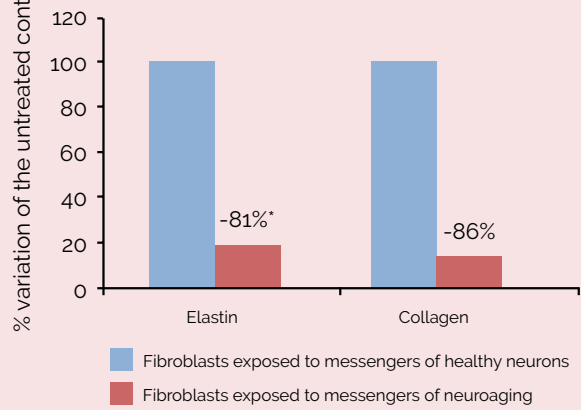
Results: Viability of neurons exposed to neuroaging decreases by 45%



Results: Viability of fibroblasts exposed to neuroaging messengers decreases by 48%

The drop of viability confirms the hypothesis that neurons exposed to neuroaging secrete messengers which directly impact fibroblasts viability.

Consequences of Neuroaging on the proteins of the Extra-Cellular Matrix



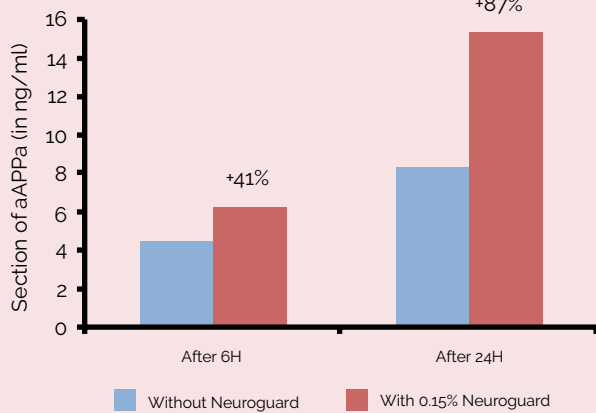
Results: Toxicity of neuroaging triggers a drop of collagen and elastin synthesis:

- Decreases collagen synthesis by -86%
- Decreases elastin synthesis by -81%

When they are exposed to neuroaging, nerves release messengers that directly impact fibroblasts viability. The communication between nerves and fibroblasts becomes toxic and accelerates skin aging.

IN VITRO TEST: NEUROGUARD PROTECTS NEURONS FROM NEUROAGING

Effect of Neuroguard on the synthesis of the neuroprotector aAPPa

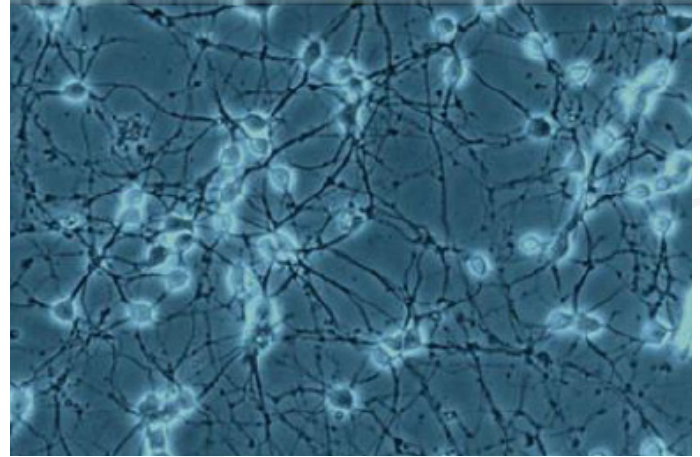


Results: Neuroguard increases the production of neuroprotector sAPP by 87%

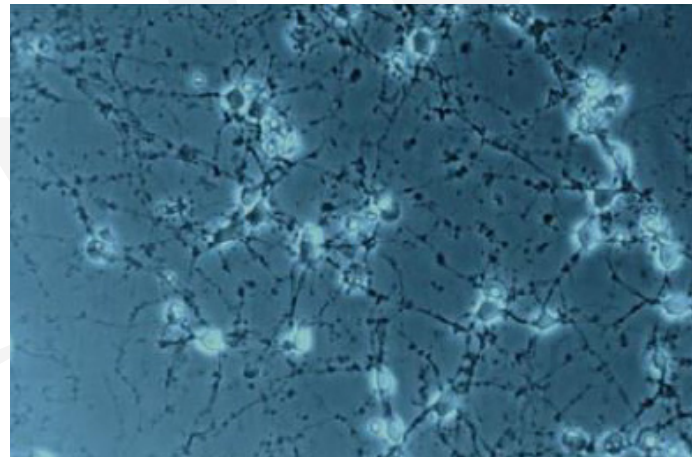
Meanwhile, Neuroguard provides 42% protection against H₂O₂ toxicity on neurons viability. Indeed, it has been demonstrated that the accumulation of free radicals leads to the gradual imbalance that appears with age between the neuroprotector sAPPa and the neurotoxic Ab.

IN VITRO TEST: NEUROGUARD PROTECTS NEURONS FROM NEURODEGENERATION

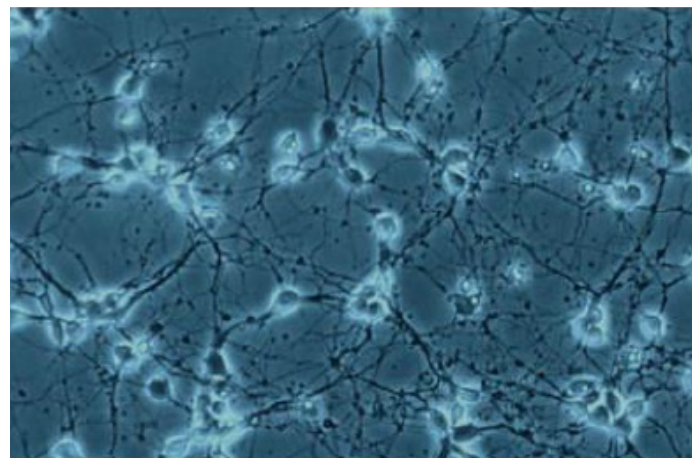
Whereas neurons which have not been exposed to neuroaging show active synapses, an extensive network and integral cell nuclei, the effect of neuroaging is characterized by fragmented nerve endings, "burntout" nuclei and a limited network. By stimulating the sAPP neuroprotector, Neuroguard enables recovering the characteristics of neurons that have not been exposed to neuroaging.



Culture of healthy neurons



Culture of neurons submitted to neuroaging



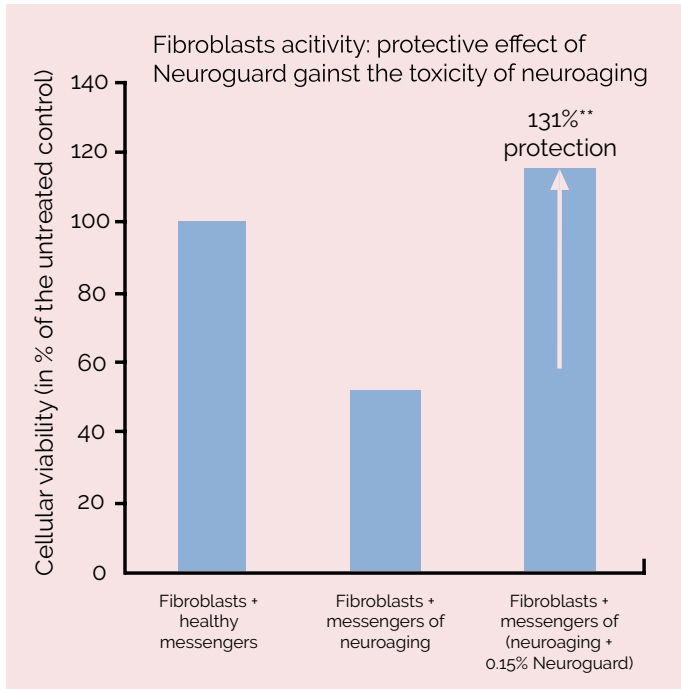
Culture of neurons submitted to neuroaging with 0.15% Neuroguard

IN VITRO TEST: NEUROGUARD PREVENTS AND PROTECTS FROM NEUROAGING

The protective action of Neuroguard on neurons viability is effective when it is used before neuroaging starts as well as when neuroaging is already underway.

- **34% protection** when Neuroguard is used **while Neuroaging starts**
- **45% protection** when Neuroguard is used **before Neuroaging starts**
- **52% protection** when Neuroguard is used **before and while Neuroaging starts**

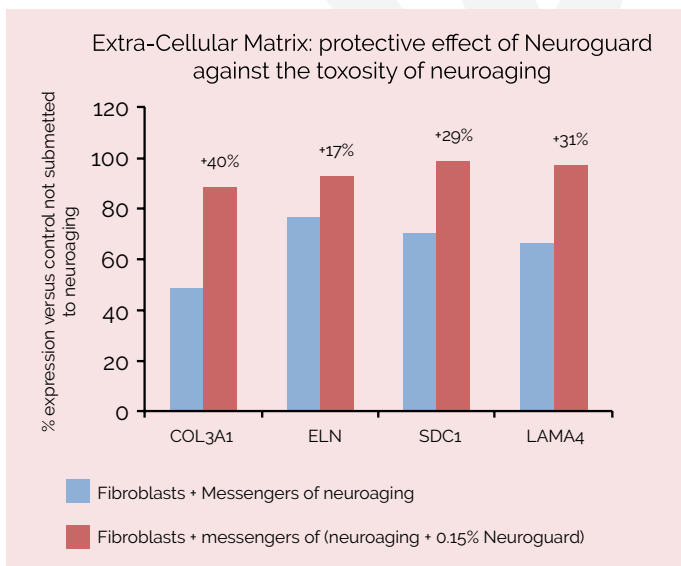
IN VITRO TEST: NEUROGUARD PREVENTS AND PROTECTS FROM NEUROAGING



Results: 131% protection of fibroblasts activity

Neuroguard protects the communication between nerves and fibroblasts from the toxicity of neuroaging and preserves fibroblasts activity

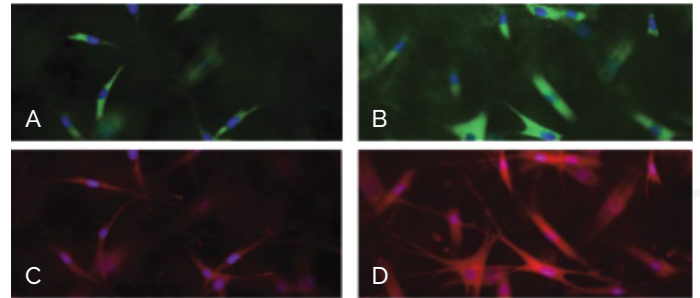
IN VITRO TEST: NEUROGUARD PROTECTS THE EXTRA-CELLULAR MATRIX FROM THE TOXICITY OF NEUROAGING



Results: By protecting the activity of fibroblasts from neuroaging toxicity, Neuroguard reactivates the expression of genes coding for ExtraCellular Matrix proteins:

- +40% Collagen III
- +17% Elastin
- +29% Syndecan
- +31% Laminin IV

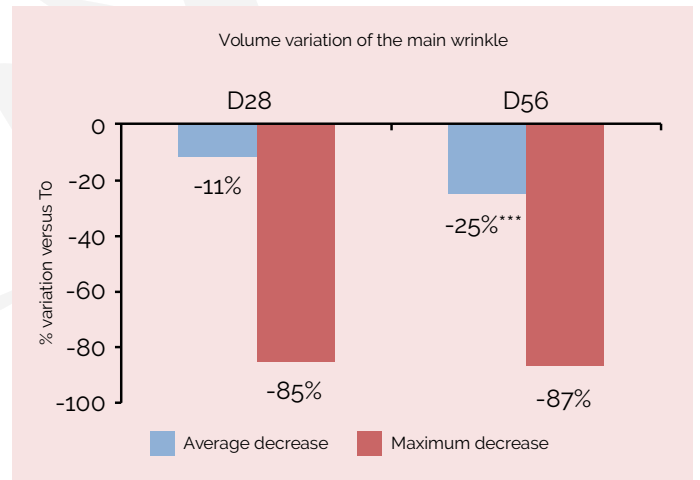
IN VITRO TEST: NEUROGUARD PROTECTS THE SYNTHESIS OF COLLAGEN AND ELASTIN FROM NEUROAGING TOXICITY



Results:

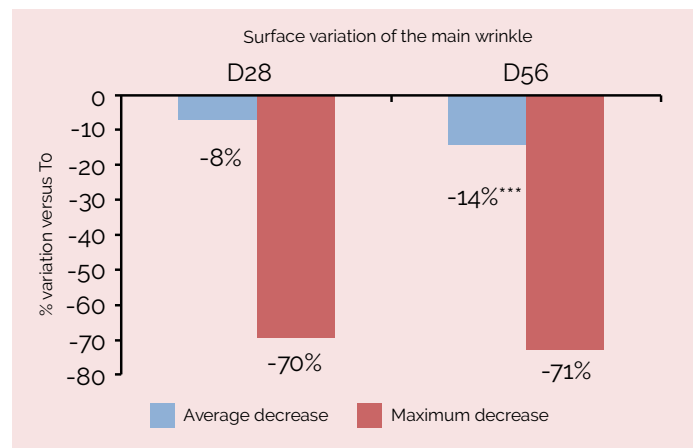
- +405% Collagen synthesis
- +832% Elastin synthesis

IN VIVO TEST: EFFICACY OF NEUROGUARD ON DEEP WRINKLES



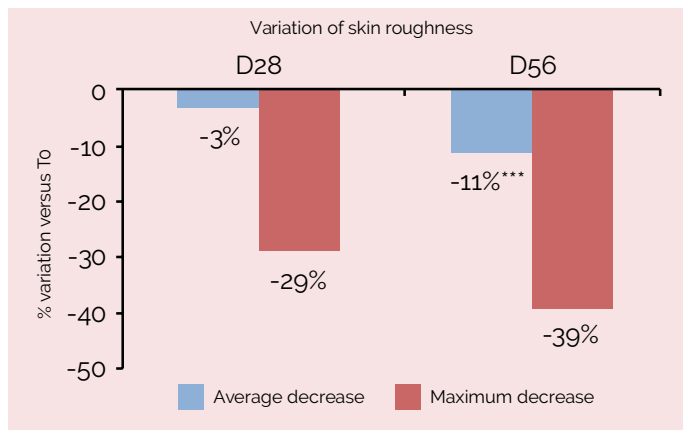
Results: Effect of Neuroguard on the volume of Crow's feet wrinkles

- After 28 days treatment: -11% and up to -85%
- After 56 days treatment: -25% and up to -87%



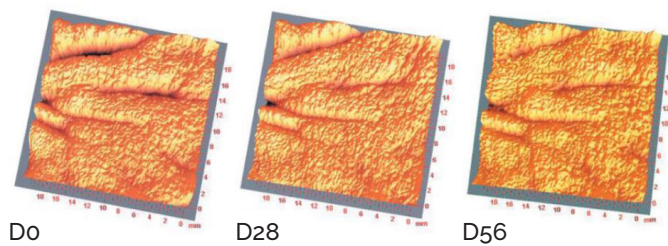
Results: Effect of Neuroguard on the area of Crow's feet wrinkles

- After 28 days treatment: -8% and up to -70%
- After 56 days treatment: -14% and up to -71%



IN VIVO TEST: VISUALIZATION OF THE EFFICACY OF NEUROGUARD ON DEEP WRINKLES

Decrease in the volume and area of Crow's feet wrinkles



Overall efficacy



Neuroguard revolutionizes neurocosmetic by directly targeting the aging of nerve endings. Its neuroprotective action blocks neuroaging and re-establishes a healthy communication between nerves and fibroblasts, thus protecting dermal cells from premature aging. Under these conditions, collagen and elastin synthesis are reactivated, deep wrinkles are diminished and skin texture is smoother.

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