

# WISEGRADE<sup>TM</sup>

EMBRACE THE WISE GRADIENT



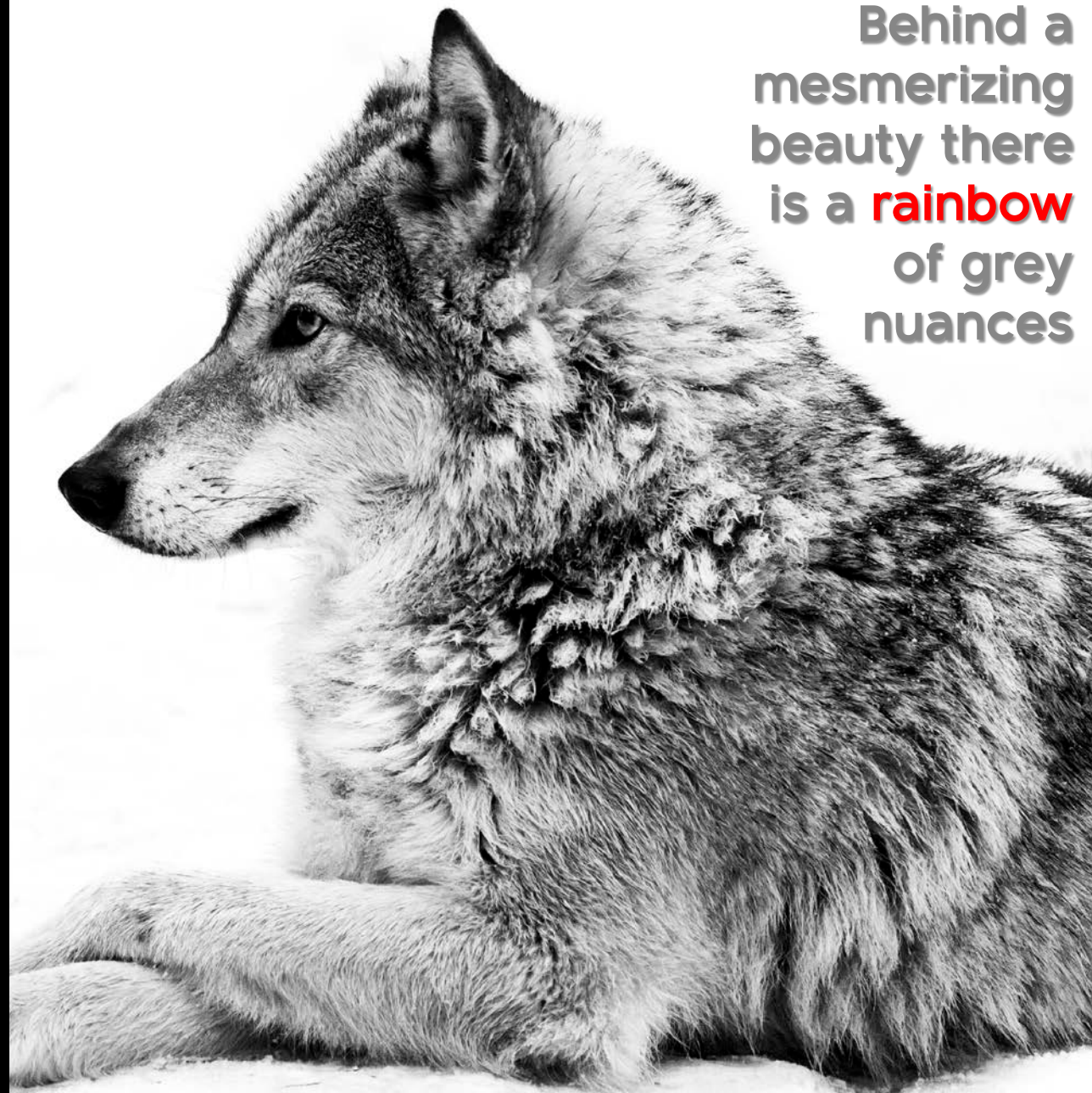


## Life is a gradient of colors

Gradient of colors in leaves marks the **seasons**, in fruits the **maturity grade** and in some flowers even the **time of day**



Behind a  
mesmerizing  
beauty there  
is a **rainbow**  
of grey  
nuances



## Listening social media, embracing the grey gradient

Social listening is the monitoring of social media channels for customers feedback regarding your company or specific topics followed by an analysis to gain insights and detect opportunities

"'Grombre' trend inspires **Instagram** community to champion naturally graying hair"

- Fox news, 2020 -

"This controversial beauty trend is up by 879% according to **pinterest**"

- Marie Claire, 2019 -

"Coronavirus: Embracing grey roots in **lockdown**"

- BBC news, 2020 -

"Grey hair is one of the **hottest trends of 2020**. Top 5 styles to follow right now"

- Hindustan Times, 2020 -





"I wish I had **more pepper** than salt. Dying is not an option"

"I love to let my **silvers shine**. Now I feel free. It's more me"

"My hair color does not decide how professional I am. I **don't want to damage** it anymore"

"I am **young**, beautiful and grey. My **glitter highlights** tell interesting stories"

### Silver foxes

Like a good red wine, they improve with age  
They are considered attractive, charming & sexy

### "Going grey" movement

Empowered women, defying society's beauty standards & embracing their natural grey color  
During the lockdown some have taken the plunge and there is no turning back

## Which are their needs?

Women who are going grey seek to mask the transition (highlights, hats, braids, stripping the dye, cut...).

White hair may turn yellow due to the use of heat (irons and dryers), tap water, solar exposition and pollution.

The oxidative stress generated oxidizes keratin proteins and the little melanin that grey hairs still have.

Silver ladies use purple or blue shampoos & conditioners to avoid oxidation by heavy metals of tap water.

They also use UV & heat protectors to avoid yellowing, without giving up styling and fun.



"I like to play with temporary colors"



"I like to style my hair, and keep it healthy"



"My hair rocks when there is no yellowing"



"I want to blend my regrowth"



“**Matching** my beard with my hair”



“Sorry! Just **not ready** yet”



“Still **silver**, still wise”



“I love to **play** with my natural hair color”



“Back to the **roots**”

How can a product  
graduating **grey** may  
help?

- Repigmenting first silvers
- No more yellowing
- Graduating the amount of grey
- Making demarcation line less visible while transitioning
- Between dying appointment

# Going grey

**Hair follicles** are independent miniorgans that anchor into the skin. The base of the hair follicle is known as the bulb, which is where the hair shaft grows

The follicle's cycles are not synchronized so hair shafts do not grey at the same time

Each new hair after the first 10 cycles has less or none pigment

In the anagen phase, there is an increase of ROS that oxidizes melanocytes, keratinocytes and fibroblasts (follicular melanocytes age faster than keratinocytes and epidermal melanocytes)

## PIGMENT LOSS

(aging, stress, environmental factors)

### REDOX HOMEOSTASIS

↑ **oxidative stress** due to melanogenesis plus emotional stress & external factors

↓ antioxidant

↑ H<sub>2</sub>O<sub>2</sub>

### STEM CELLS

↓ **melanocyte stem cells (MSCs)** migrate into the bulb (apoptosis or ectopic differentiation in the bulge)

↓ antiapoptotic factors

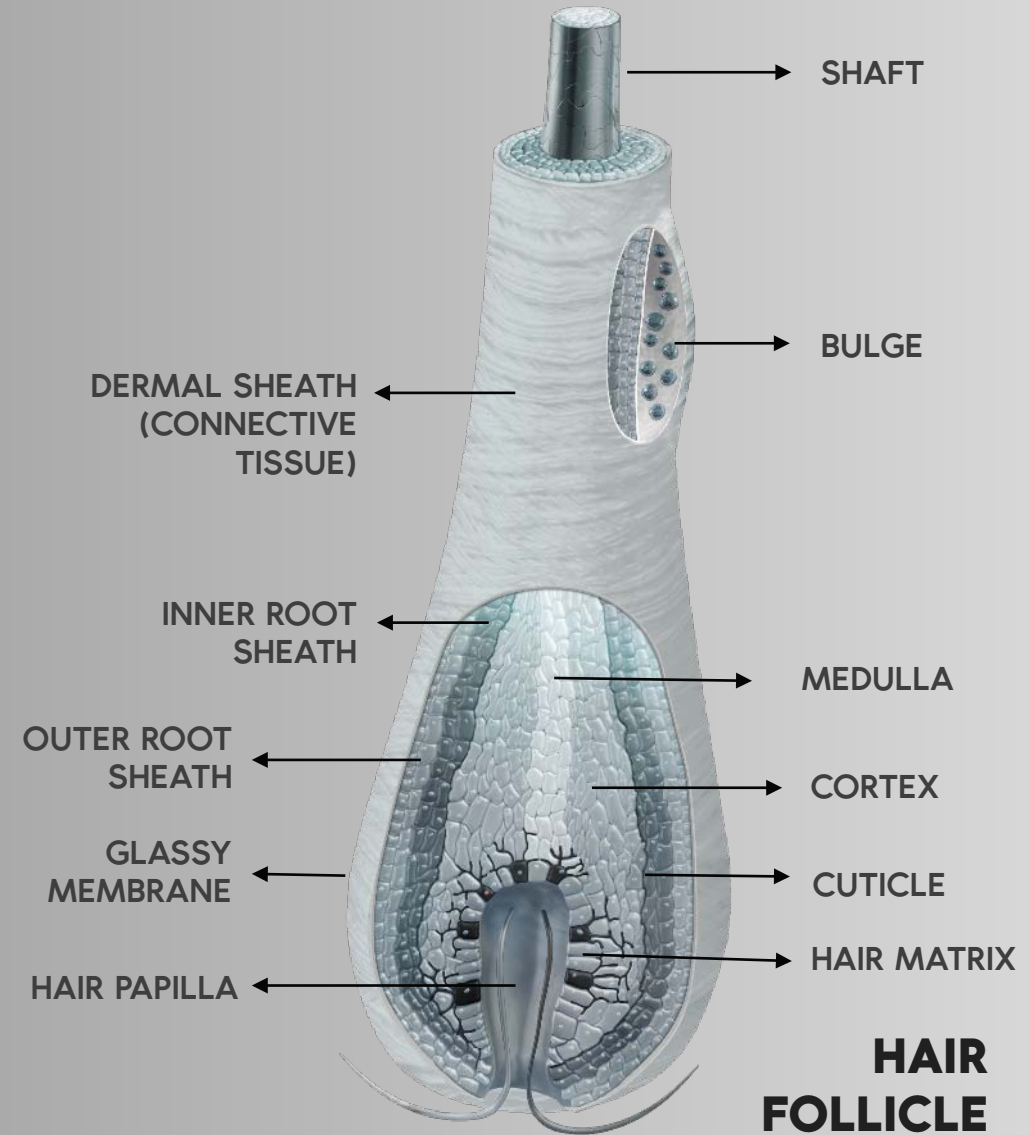
↓ MSCs migration

### MELANOGENESIS

↓ **functional melanocytes** in the bulb

↓ tyrosinase activity

↓ melanosome transfer

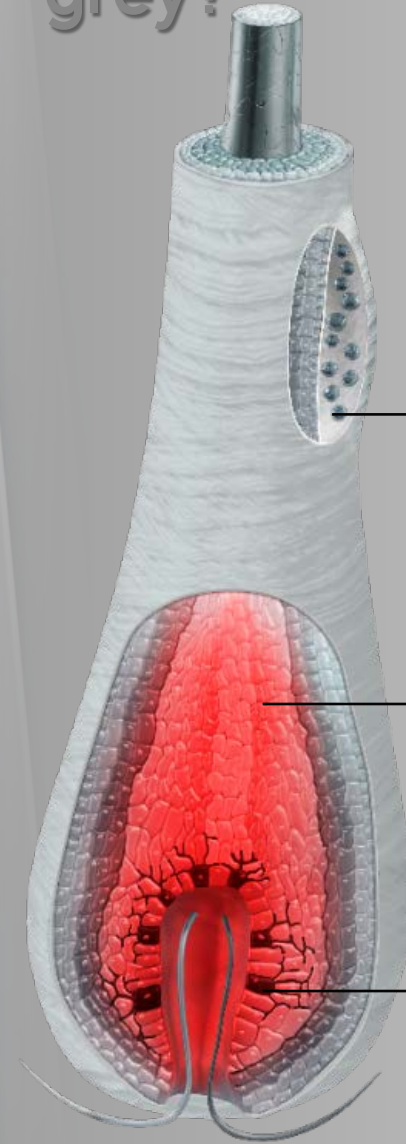


**HAIR FOLLICLE**



# Is it possible to graduate grey?

Wisegrade™ is a **plant-GMCSF** protein from the **Wild Plants Technology** platform. GMCSF reacts with its melanocyte receptor, activating multiple MITF pathways inducing melanogenesis, antioxidants, and stem cell protecting factors



## REDUCING OXIDATIVE STRESS

↑ antioxidants

↑ antiapoptotic factors

## IMPROVING STEM CELL MAINTENANCE

↓ MSCs apoptosis

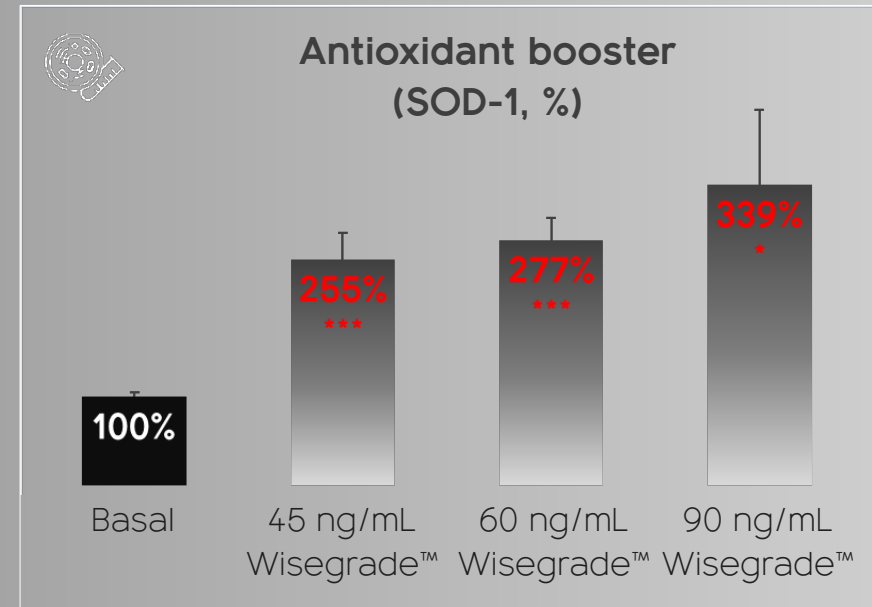
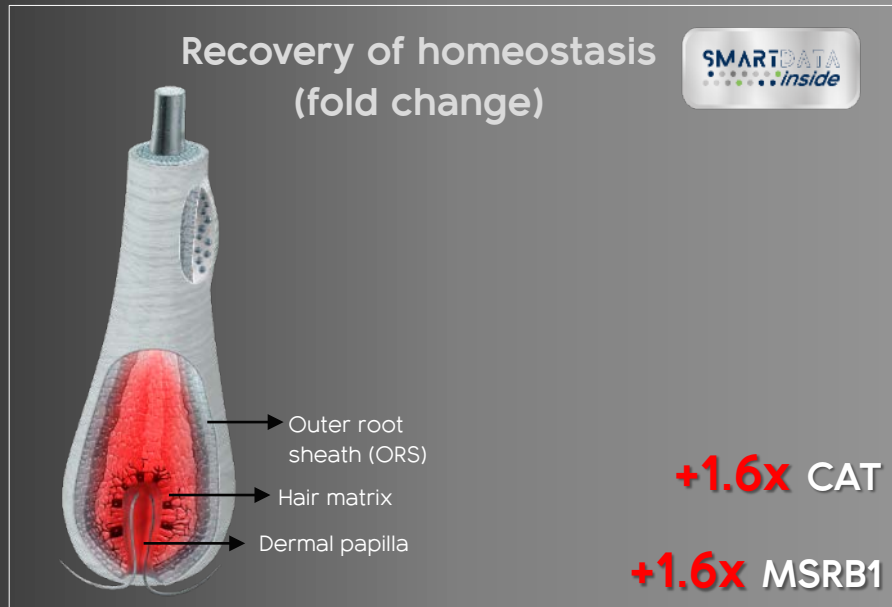
## STIMULATING MELANOGENESIS

Amelanotic melanocytes in the ORSs may migrate and differentiate into melanogenic melanocytes **under certain stimuli**

↑ **functional melanocytes**

# Recovering redox homeostasis

CAT is an **antioxidant** that decomposes  $H_2O_2$   
 MSRB1 **repairs proteins** damaged by oxidative stress (e.g. tyrosinase)  
 SOD-1 is an **antioxidant** that decomposes superoxide radical

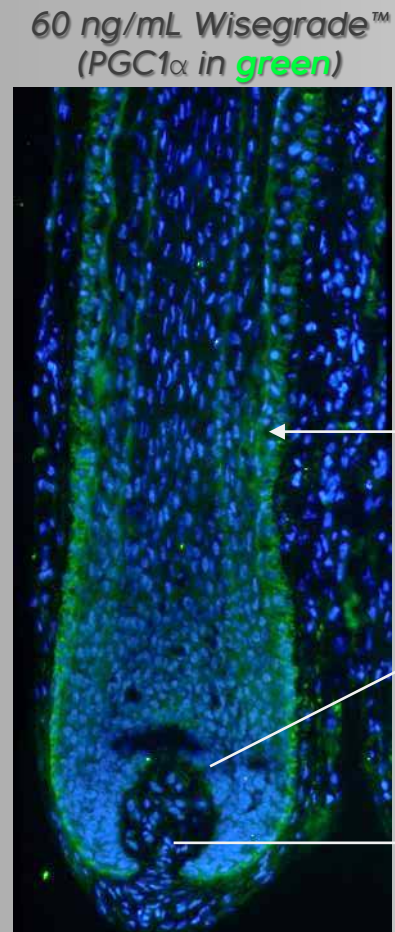
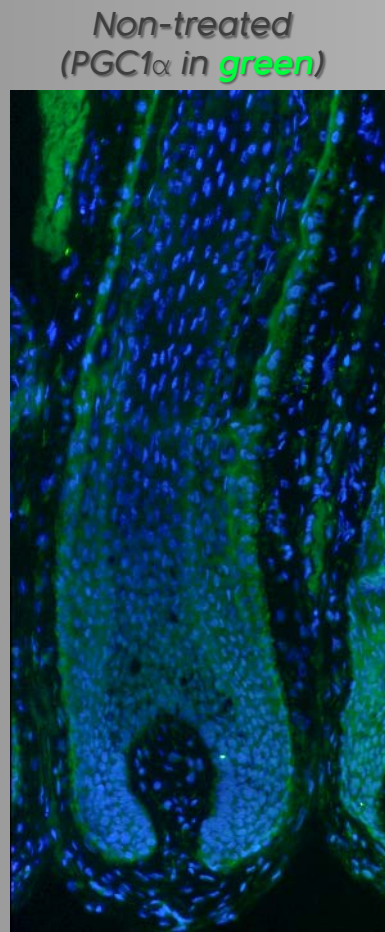
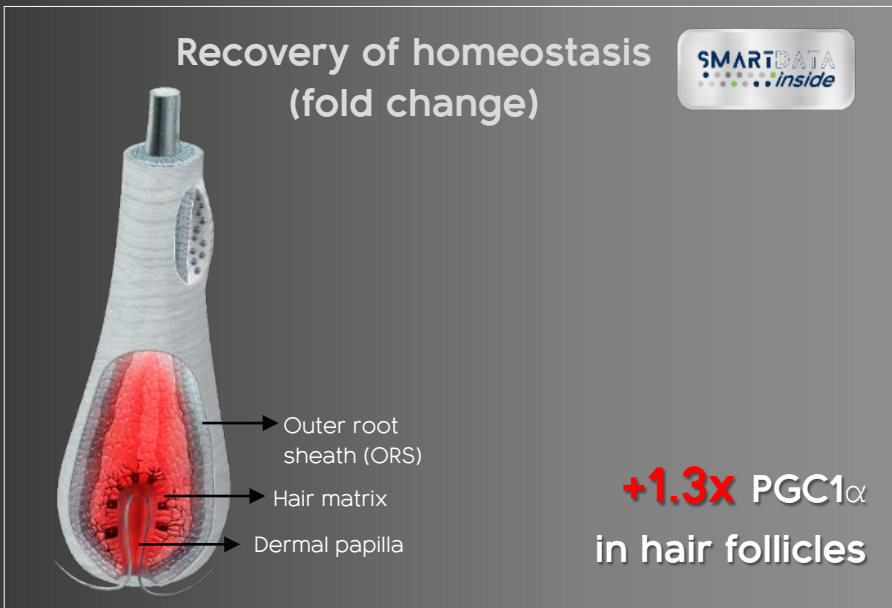


- Human Epidermal Melanocytes neonatal moderately pigmented (HEMn-MP)
- 60 ng/mL Wisegrade™ active ingredient which corresponds to 2% Wisegrade™
- qPCR (quantitative PCR)
- 24 h
- CAT (Catalase)
- MSRB1 (Methionine sulfoxide reductase B1)

- HEMn-MP
- 45 ng/mL Wisegrade™ active ingredient corresponds to 1.5% Wisegrade™
- 90 ng/mL Wisegrade™ active ingredient corresponds to 3% Wisegrade™
- 24 h
- Colorimetry
- SOD-1 (Superoxide dismutase-1)

# Recovering redox homeostasis

PGC1 $\alpha$  is a positive regulator of mitochondrial biogenesis and respiration, induces the expression of ROS detoxifying enzymes such as SOD and GPX, and is activated by MITF



- Human scalp hair follicles in anagen VI phase (HF, 50 years old)
- 60 ng/mL Wisegrade™ active ingredient corresponds to 2% Wisegrade™
- qPCR (quantitative PCR)
- 24 h
- PGC1 $\alpha$  or PPARGC1 $\alpha$  (Peroxisome proliferator-activated receptor gamma coactivator 1-alpha): encodes PGC1 $\alpha$

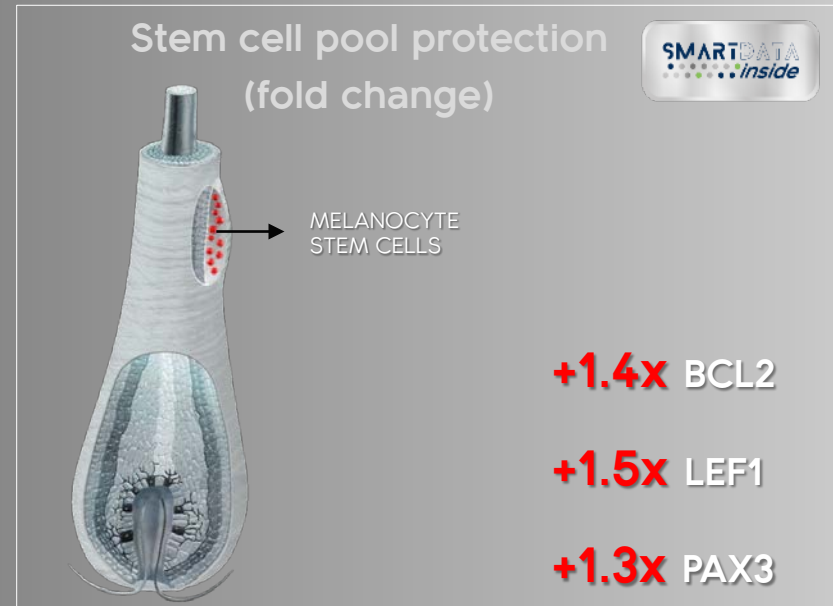
- Human scalp hair follicles in anagen VI phase (HF, 50 years old)
  - Wisegrade™ active ingredient (60 ng/mL)
    - 48 h
- Immunofluorescence

# Protecting the stem cells pool

BCL2 is an **antiapoptotic factor** that is critical for the survival of melanocytes and MSCs

LEF1 is involved in **melanocyte survival**

PAX3 prevents terminal differentiation

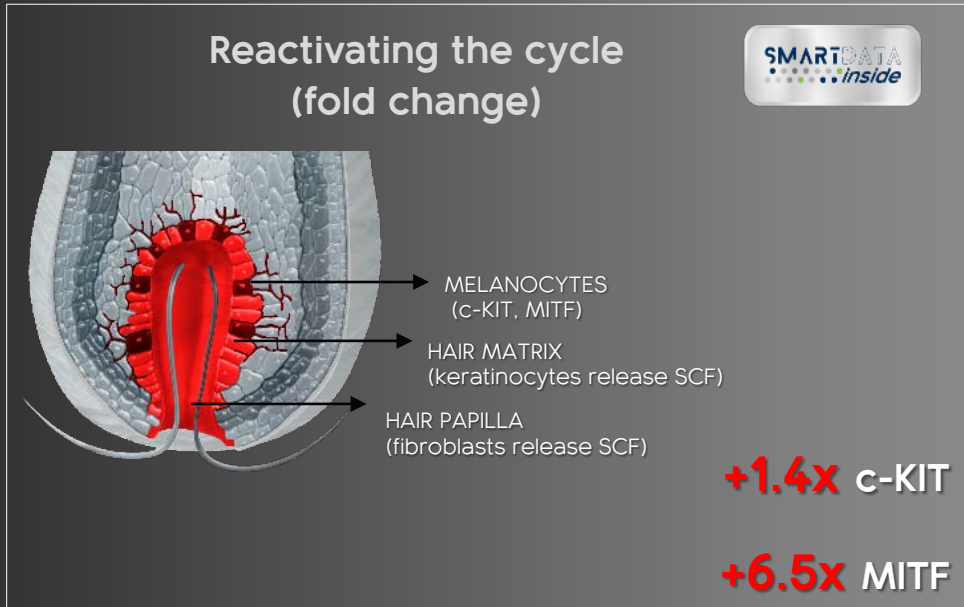


- Human Epidermal Melanocytes neonatal darkly pigmented (HEMn-DP)
  - Wisegrade<sup>™</sup> active ingredient (20 ng/mL)
    - qPCR (quantitative PCR)
      - 24 h
        - BCL2 (BCL2 apoptosis regulator)
  - LEF1 (Lymphoid enhancer binding factor 1)
    - PAX3 (Paired box 3)

# Reactivating the cycle

Dermal cells release Stem Cell Factor (SCF) that binds to its receptor c-KIT activating MITF by phosphorylating it

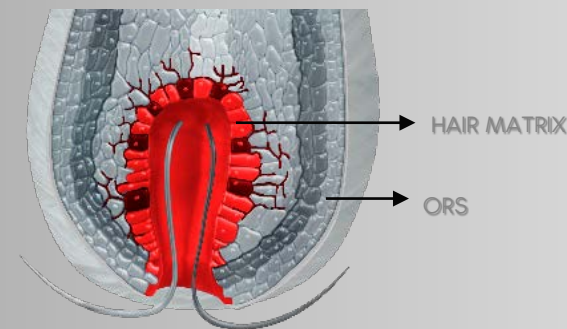
MITF is a master regulator of genes involved in melanocyte proliferation, survival, differentiation, apoptosis, redox homeostasis and melanogenesis



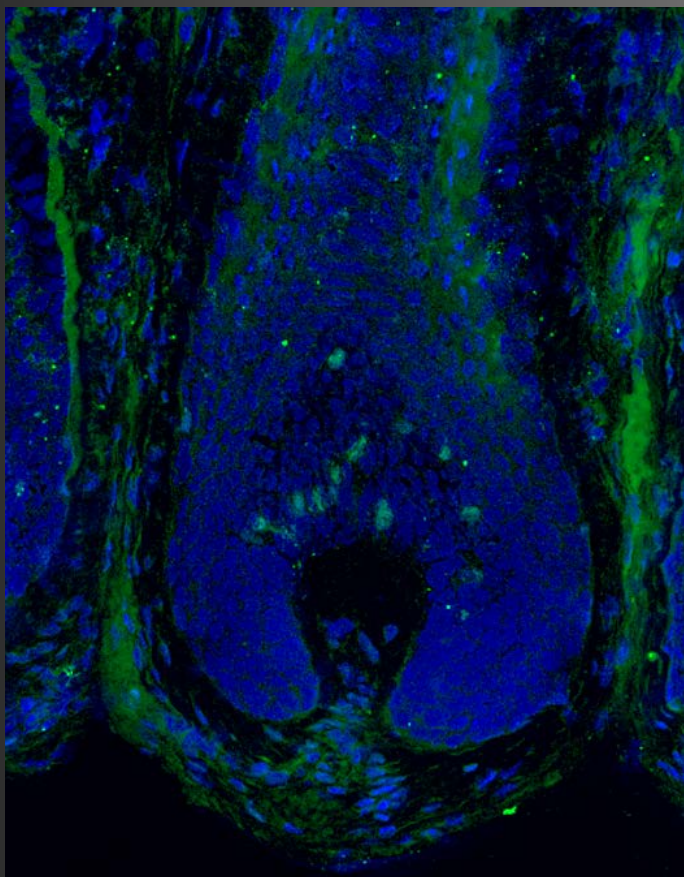
- Human Epidermal Melanocytes neonatal darkly pigmented (HEMn-DP)
- Wisegrade™ active ingredient (20 ng/mL)
- qPCR (quantitative PCR)
- 24 or 48 h
- c-KIT (KIT proto-oncogene receptor tyrosinase kinase)
- MITF (Melanocyte inducing transcription factor)



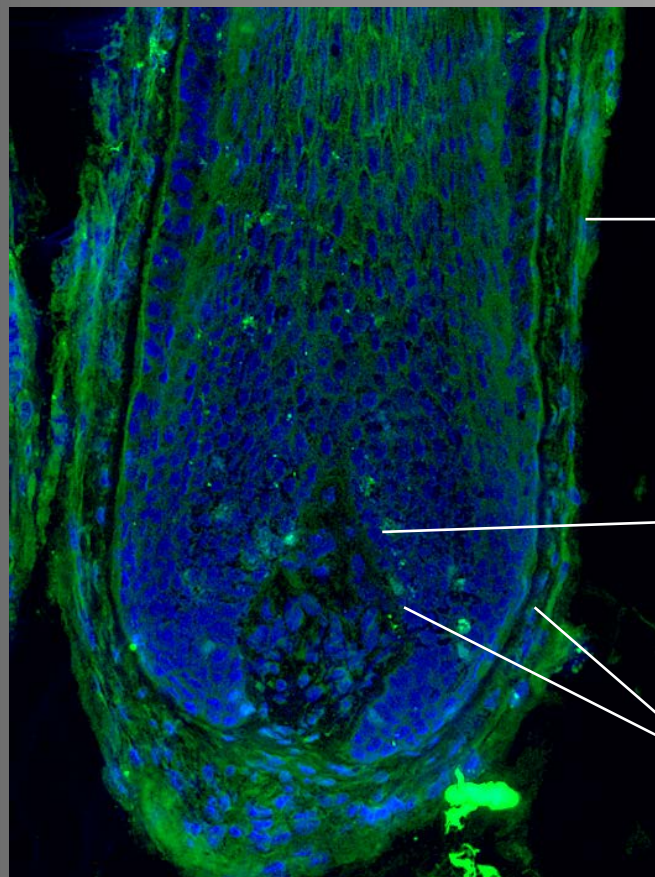
# Reinforcing melanogenesis master regulator



Non-treated (MITF in green)



60 ng/mL Wisegrade<sup>™</sup> (MITF in green)



**+12%** MITF (protein)  
in ORS

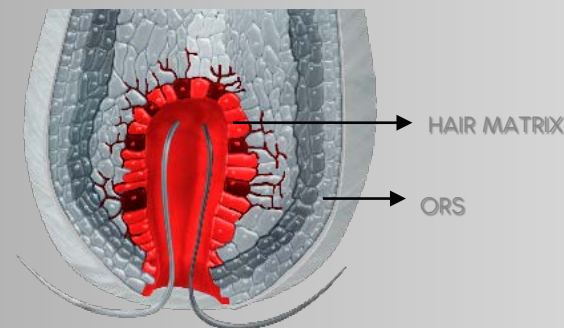
**+37%** MITF (protein)  
in hair matrix

**+40%** cells containing  
MITF in hair matrix & ORS

- Human scalp hair follicles in anagen VI phase (HF, 50 years old)
- 60 ng/mL Wisegrade<sup>™</sup> active ingredient corresponds to 2% Wisegrade<sup>™</sup>
  - 48 h
- Immunofluorescence



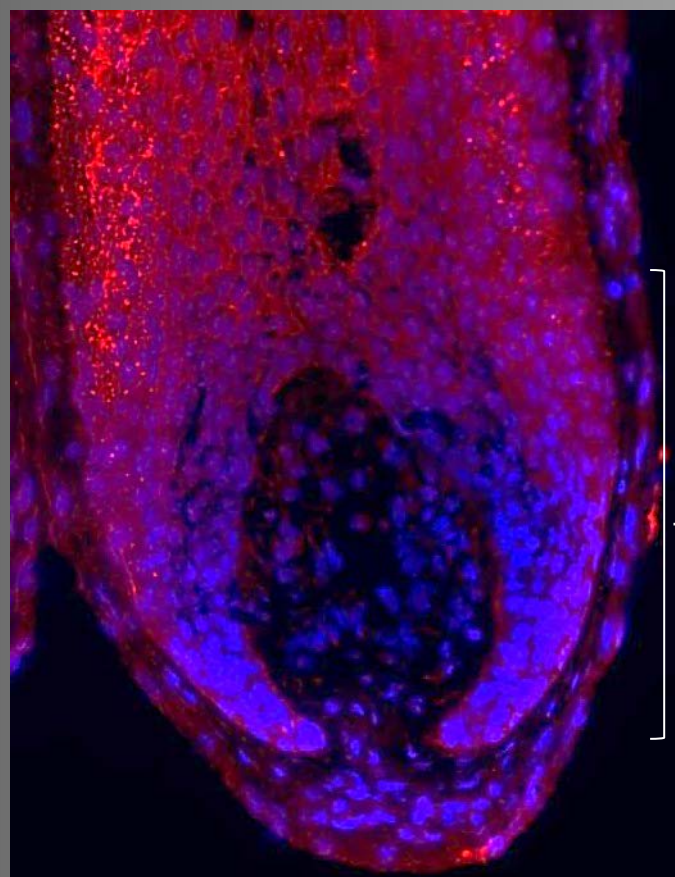
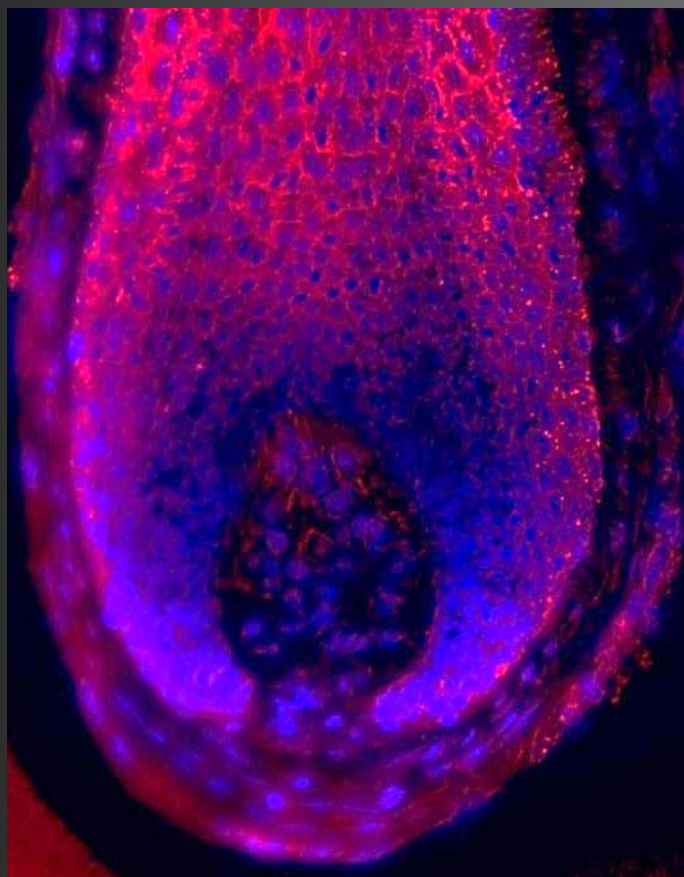
# ...and melanogenesis begins



MITF phosphorylation activates survival, differentiation, apoptosis and redox homeostasis

Non-treated (activated MITF+ in red)

60 ng/mL Wisegrade™ (activated MITF+ in red)



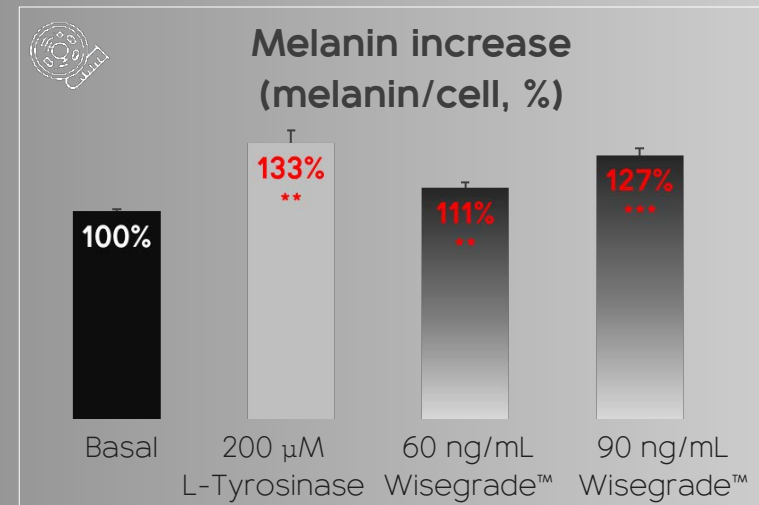
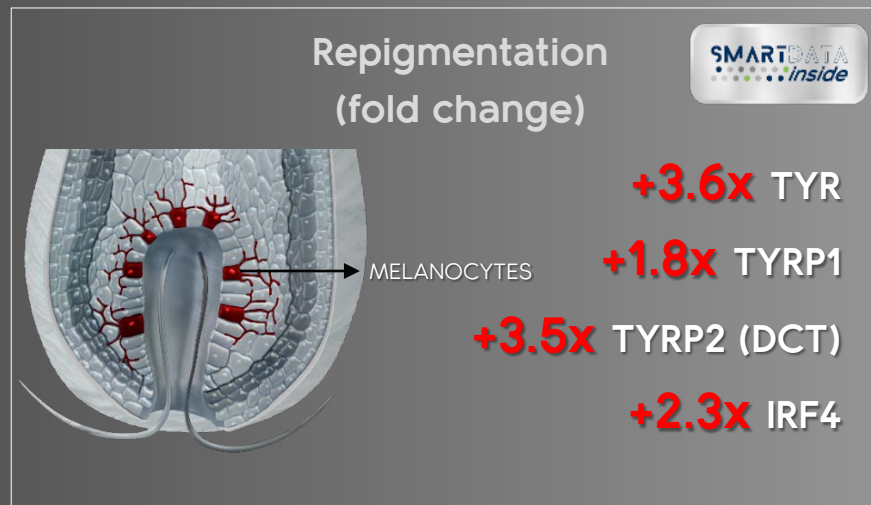
**+180%** cells containing activated MITF+ (phosphorylated) in hair bulb

- Human scalp hair follicles in anagen VI phase (HF, 50 years old)
- 60 ng/mL Wisegrade™ active ingredient corresponds to 2% Wisegrade™
  - 48 h
- Immunofluorescence



# Repigmentation

TYR, TYRP1 and TYRP2 are essential enzymes involved in **melanin biosynthesis**. IRF4 cooperates with MITF to activate the expression of **TYR**.



Basal

200 μM L-Tyrosine

90 ng/mL Wisegrade<sup>TM</sup>



- Human Follicle Dermal Papilla cells (HFDPC)
- Wisegrade<sup>TM</sup> active ingredient (50 ng/mL)
- qPCR (quantitative PCR)
- 24 h
- IRF4 (Interferon regulatory factor 4))

- Human Epidermal Melanocytes neonatal darkly pigmented (HEMn-DP)
- Wisegrade<sup>TM</sup> active ingredient (20 ng/mL)
- qPCR (quantitative PCR)
- 48 h
- TYR (Tyrosinase), TYRP1 (Tyrosinase related protein 1), TYRP2 (DCT) (Dopachrome tautomerase)

- HEMn-MP
- 60 ng/mL & 90 ng/mL Wisegrade<sup>TM</sup> active ingredient corresponds to 2% & 3% Wisegrade<sup>TM</sup>
- 72 h
- Spectrophotometry
- Microscopy
- \*\*\*p<0.001 vs T0, \*\*p<0.01 vs basal



# Reinforcing the integrity of melanosomes

PMEL17 is involved in **melanin synthesis**, stabilization of melanin intermediates and acts as a scaffold in melanosomes for the deposition of melanin.

MLANA is involved in **melanosome biogenesis**.

Reinforcing the integrity of melanosomes (fold change)

SMARTDATA  
inside



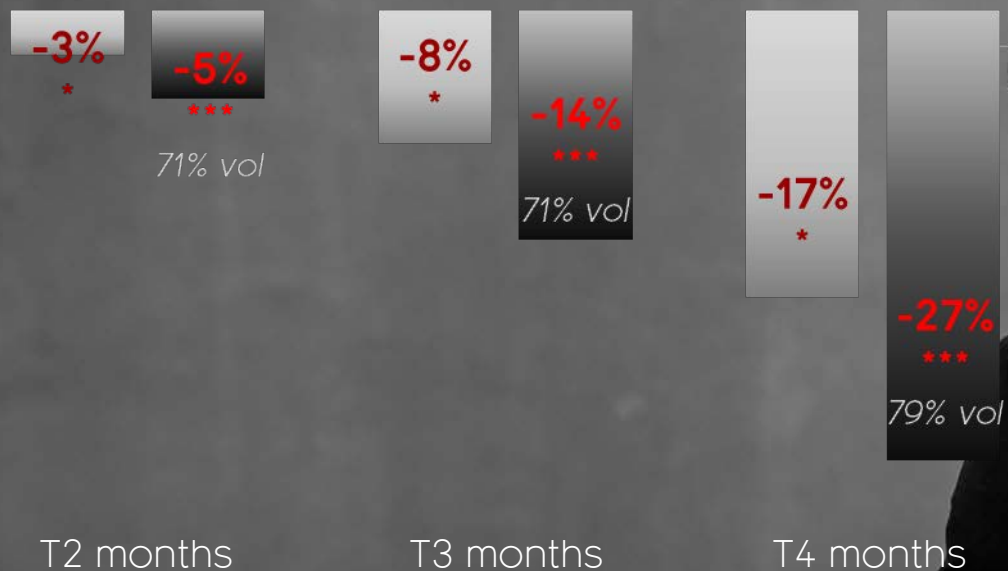
**+4.5x** PMEL17

**+1.6x** MLANA

- Human Epidermal Melanocytes neonatal darkly pigmented (HEMn-DP)
- Wisegrade™ active ingredient (20 ng/mL)
- qPCR (quantitative PCR)
- 48 h
- PMEL17 (Premelanosome protein)
- MLANA or MART1 (Melan-A)



## Graduating grey to natural hair color (ratio, %)



Up to:  
**-34%** in 4 months



- 20 men panel (40-55 years old, salt & pepper, 14 preselected with a ratio of grey hair between 20-30%)
- Tonic with 3% Wisegrade™
- Once a day for 4 months on the scalp
- Dermatoscope
- \*\*\*p<0.001 vs T0, \*p<0.05 vs T0

# Graduating grey to natural hair color (ratio, %)

WISEGRADE™  
EMULSING THE WISE GRADIENT

**-30.4%** in 4 months



- 18 men panel (40-55 years old, salt & pepper, 14 preselected with a ratio of grey hair between 20-30%)
- Vol 14
- Tonic with 3% Wisegrade™
- Once a day for 4 months on the scalp
- Dermatoscope

T0 months



T4 months



T0 months



T4 months



# Graduating grey to natural hair color (ratio, %)

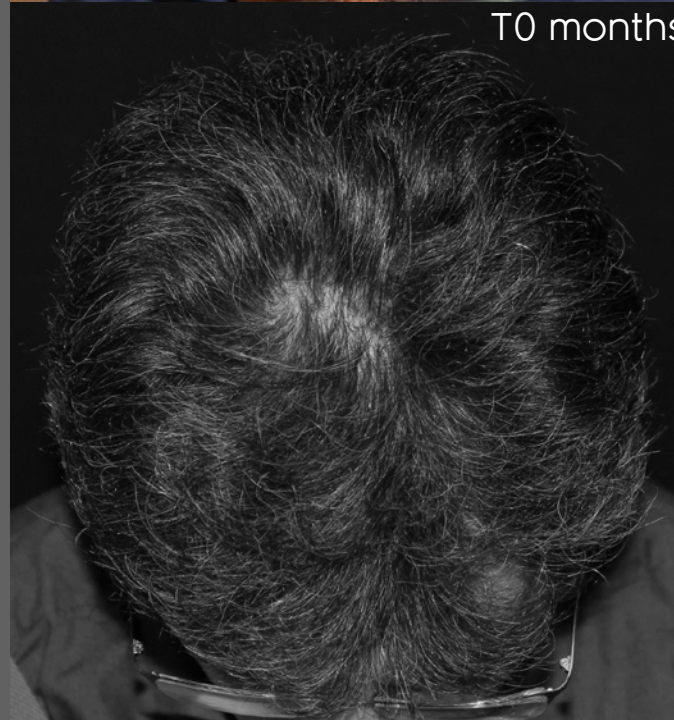
WISEGRADE™

EMBRACE THE WISE GRADIENT

**-27.8%** in 4 months



- 18 men panel (40-55 years old, salt & pepper, 14 preselected with a ratio of grey hair between 20-30%)
- Vol 18
- Tonic with 3% Wisegrade™
- Once a day for 4 months on the scalp
- Dermatoscope



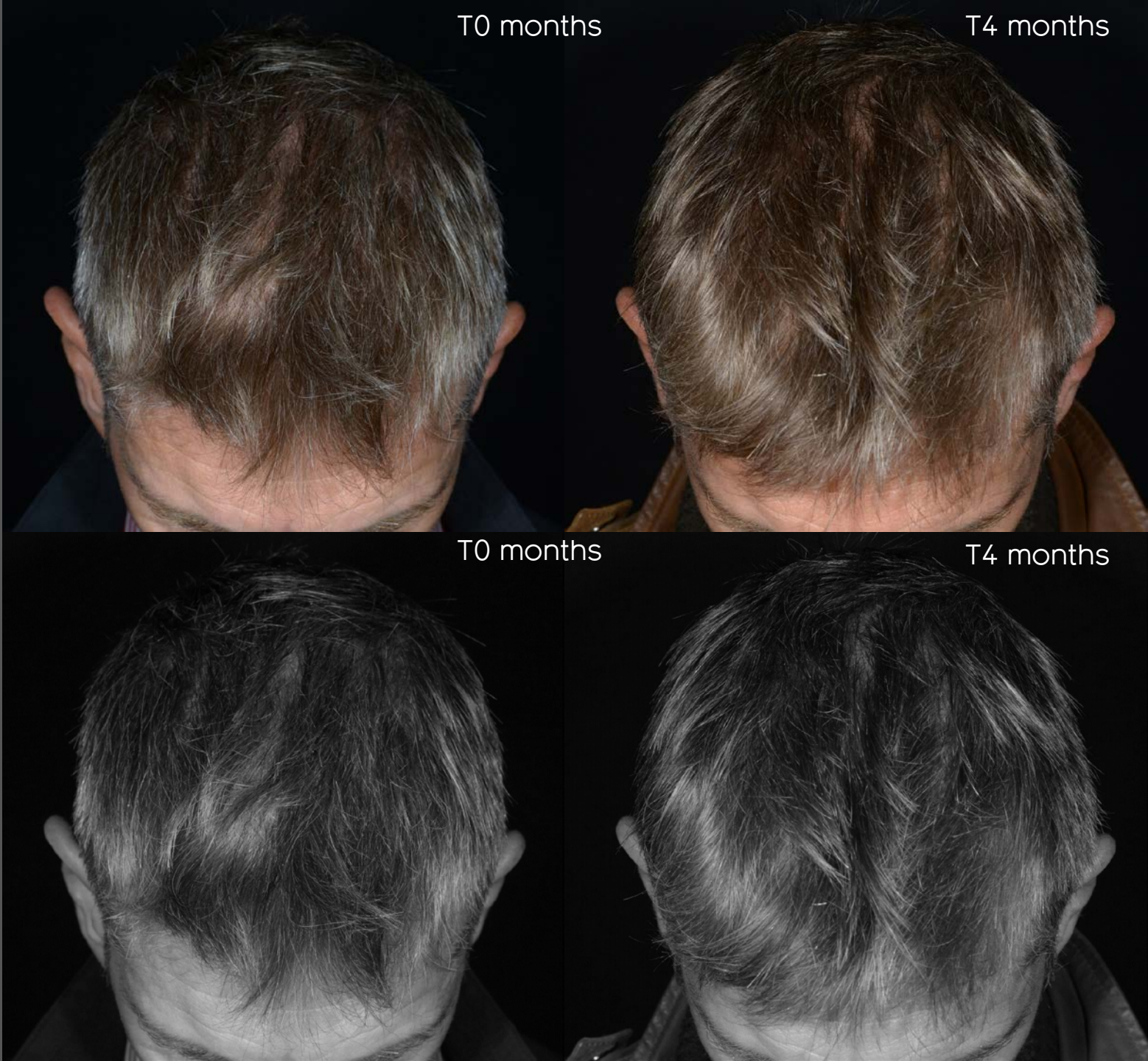
# Graduating grey to natural hair color (ratio, %)

WISEGRADE™  
EMBRACE THE WISE GRADIENT

**-27.3%** in 4 months



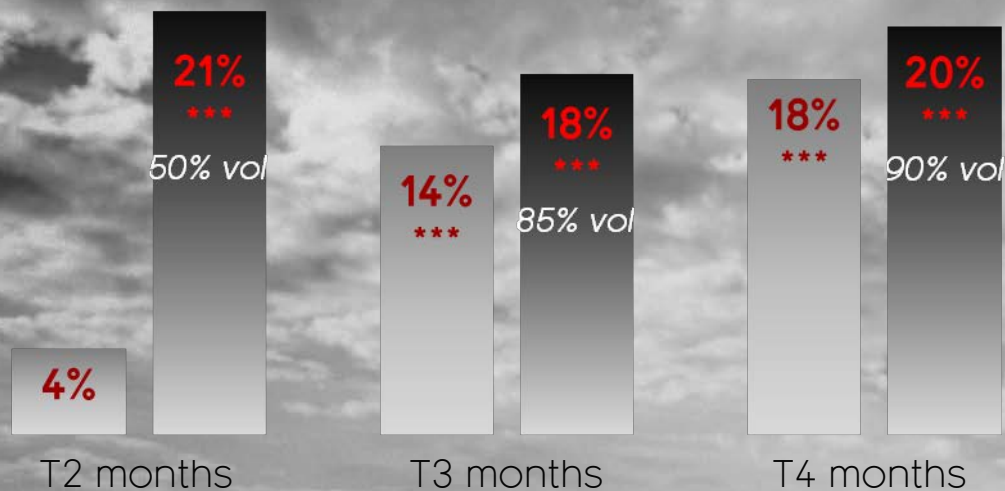
- 18 men panel (40-55 years old, salt & pepper, 14 preselected with a ratio of grey hair between 20-30%)
- Vol 11
- Tonic with 3% Wisegrade™
- Once a day for 4 months on the scalp
- Dermatoscope



# Antioxidant protection (%)

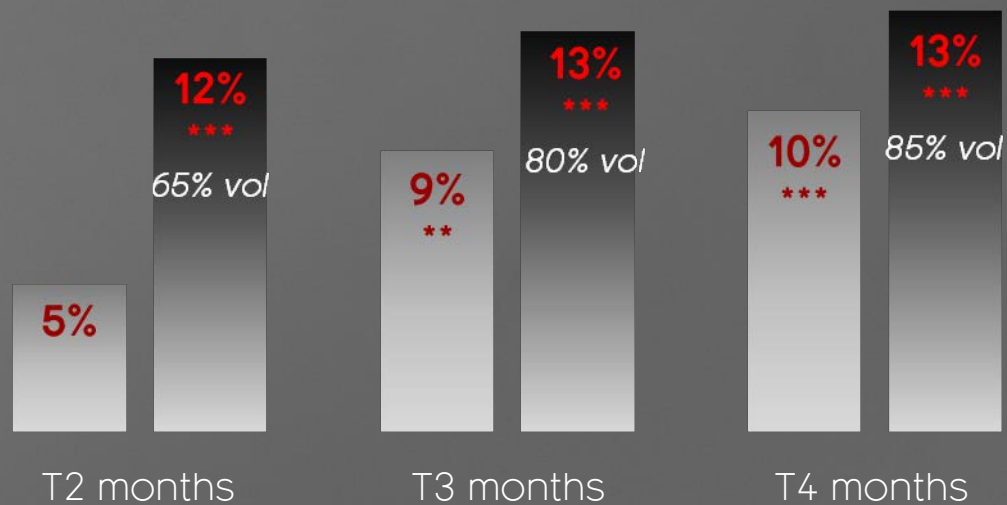
Up to:

**+45%** in 4 months



- 20 men panel (40-55 years old, salt & pepper)
- Tonic with 3% Wisegrade™
- Once a day for 4 months on the scalp
- Ferric Reducing Antioxidant Parameter (FRAP)
- \*\*\*p<0.001 vs T0

## Hair gloss (%)



Up to:

**+38%** in 2 months



- 20 men panel (40-55 years old, salt & pepper)
- Tonic with 3% Wisegrade™
- Once a day for 4 months on the scalp
- Colorimeter
- \*\*\*p<0.001 vs T0

# What do volunteers think

“Time has  
**stopped** for my  
hair”

30% volunteers

“It is **brighter**”

55% volunteers

“It has more  
**volume**”

60% volunteers

“I feel more  
**confident**”

50% volunteers

“It looks more  
**healthy**”

60% volunteers

“My hair is  
**growing faster**”

45% volunteers

“It is **stronger**”

60% volunteers



- 20 men panel (40-55 years old, salt & pepper)
- Tonic with 3% Wisegrade™
- Once a day for 4 months on the scalp
- Self-assessment



WISEGRADE™  
EMBRACE THE WISE GRADIENT

## Technical information

Product Name: **Wisegrade™**

Plant-based biotechnological  
ingredient

Recommended dose: 2-3%

INCI name of the active ingredient:  
Glycoproteins

99.99% Natural origin (ISO standard  
16128)

Readily biodegradable

Appearance: Solution

Solubility: Water soluble



IH-822/2.1/B94

# WISEGRADE<sup>3</sup>™

EMBRACE THE WISE GRADIENT

