vytrus biotech

Capilia Longa™

Make your hair sprout again

PRESERVATIVE FREE

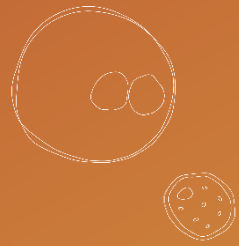
NATURAL ORIGIN 100% ISO 16128

PRESERVING BIODIVERSITY

IECIC

ECOCERT - COSMOS APPROVED

An awarded ingredient



1. Introduction

01.1 Physiology of hair bulb

01.2 Hair cycle

01.3 Dermal papilla: the orchestra director

01.4 Epigenetic reset of the hair cycle

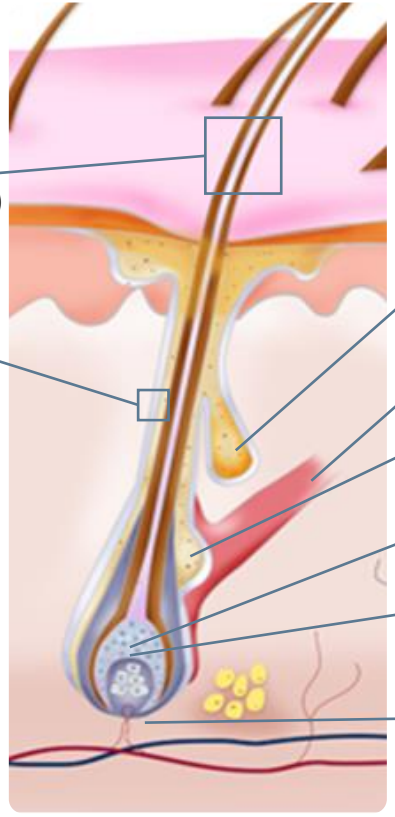
Physiology of hair bulb

Hair shaft
(medulla, cortex, cuticle)

Root sheaths
(inner & outer)

Hair Follicle

Hair Bulb



Sebaceous gland

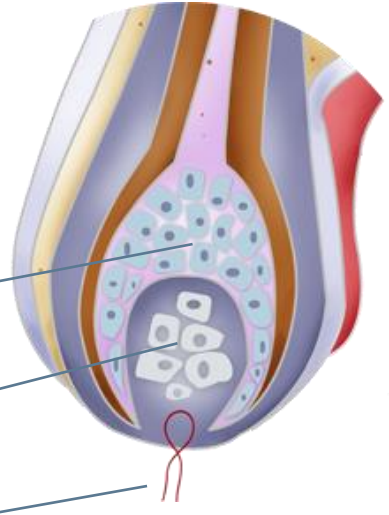
Arrector pili muscle

Bulge

Matrix

Dermal papilla

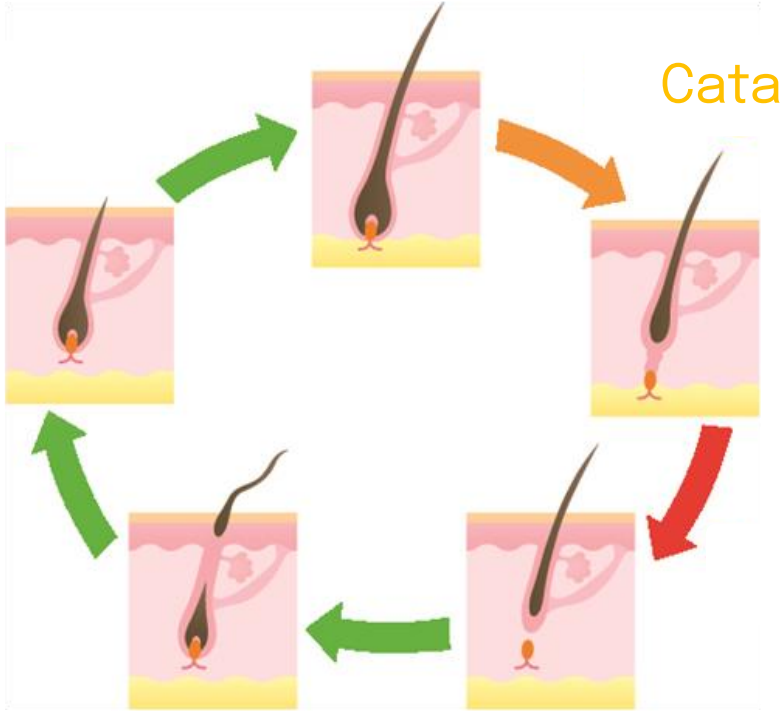
Blood capillaries



Hair cycle, a complex network

Anagen

miR-31
FGF
IGF-1
MsX2
SGK3
Shh
PI3K
Wnt
VEGF
HGF
PDGF



Catagen

miR-22
BMP
EGFs
TGFb1
FGF5
EGFR

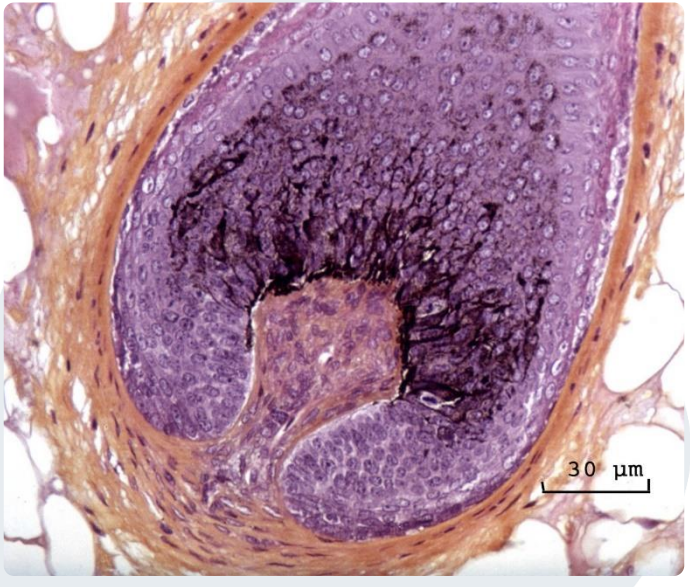
Telogen

There are many markers which activate the Anagen pase, and many markers which activate the Catagen and Telogen phases

Dermal papilla: the orchestra director

The biological interaction with Dermal Papilla is crucial for the re-activation of hair cycle and the epigenetic reset of hair bulb:

- Activates proliferation and differentiation of keratinocytes in the matrix
- Regulates the hair cycle
- Determines the quality and size of produced hair
- Can regenerate the whole hair follicle



It is one of the most rapidly proliferating tissues in the human body

Bulb “homing”: key molecules

Micro-environment around bulb

Epigenetic regulation

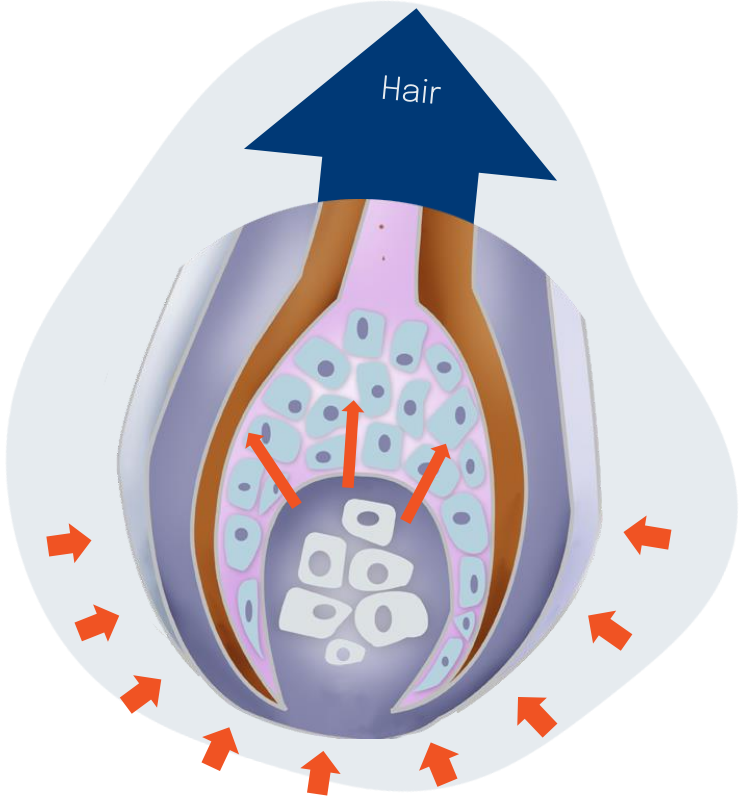
miRNA-31, miRNA-22

Growth Factors

IGF-1, TGFβ1, EGF, VEGF, etc.

Nutrients

s-Aa, oligoelements, vitamins, etc.



A complex signalling network

Epigenetic regulation miRNAs: epigenetic switchers

Small molecules of non-codifying RNA (≈20 nucleotides)

Refined control of hair cycle

Gene expression

Transcription Factors modulation

Growth Factors delivery modulation

Cell differentiation

Stem cell activation

New therapeutic target

Two new antagonist miRNAs

miRNA-31 (miR-31)

- Exclusively in Anagen phase
- Prevents the entry into the Catagen
- Promotes cell differentiation during hair growth
- Stimulates Follicle Stem Cells (FSC)
- Promotes the synthesis of hair structural keratins (14,16, 17)
- Modulates the follicle vascularisation

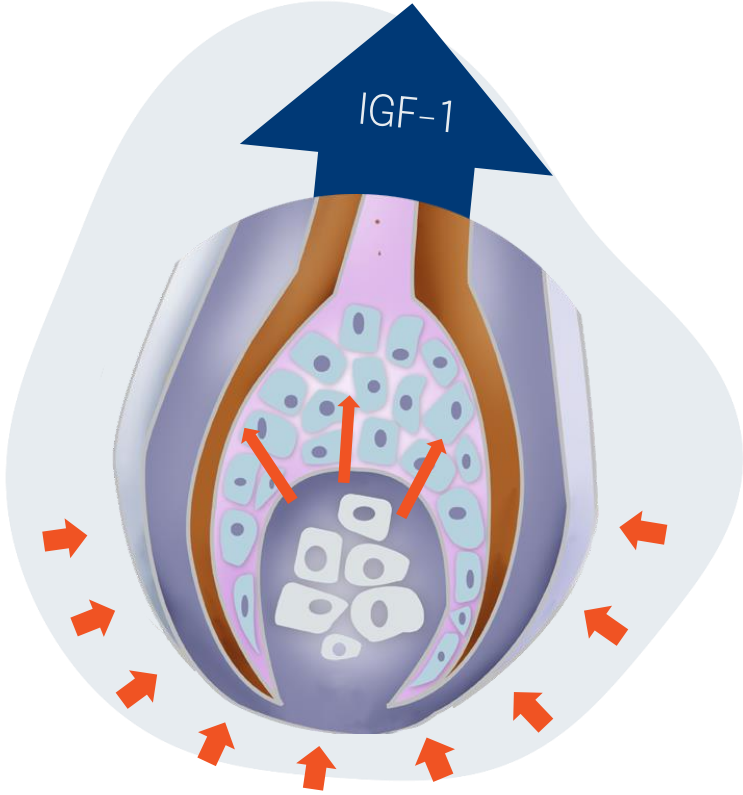
miRNA-22 (miR-22)

- Highly expressed during Catagen and Telogen phases
- Inhibits cell differentiation
- Inhibits FSC colony formation
- Inhibits the synthesis of keratins
- Promotes the apoptosis (programmed cellular death)

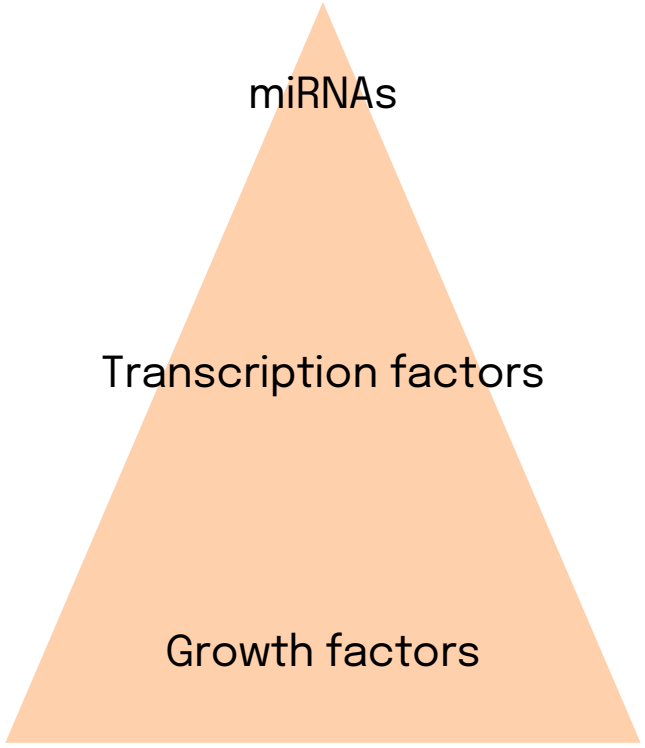
Growth factor IGF-1: a master paracrine signaler

Micro-environment around bulb

- A potent mitogenic growth factor from DP
- Key role in hair cycle regulation
- Promotes the development of hair follicle
- Maintains the Anagen phase
- Delays the entrance in Catagen phase



Epigenetic reset of the hair cycle



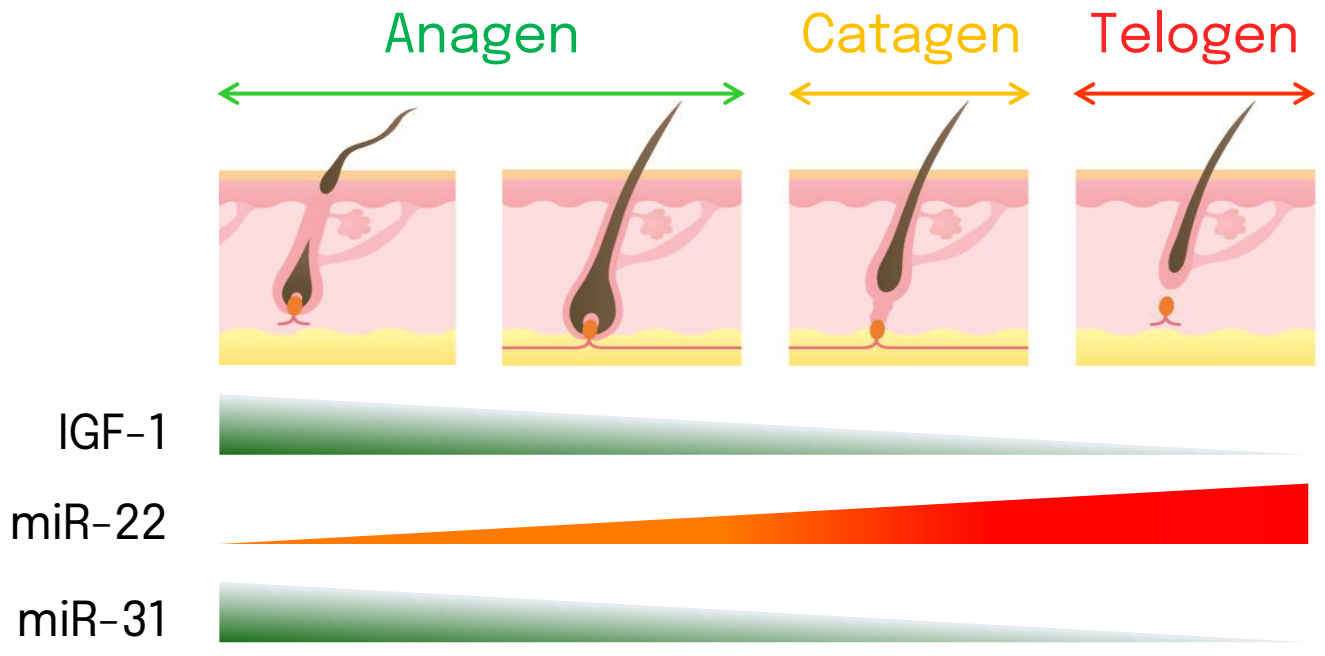
Upstream regulation: specific miRNAs activate specific transcription factors

Next regulation step: transcription factors modulate specific genes

Once the genes of Anagen phase have been activated, a cascade of growth factors is initiated

Capilia Longa™ rebalances the signalling cascade and the hair cycle

Epigenetic reset of the hair cycle



2. The plant and the active

02.1 The plant: *Curcuma longa*

02.2 The active: CAPILIA LONGA™

02.3 What if we applied plant growth factors to our hair?

02.4 The technology: Phyto-Peptidic Fractions

The plant: *Curcuma longa*

- Tropical and subtropical plant characterized by the existence of a very ramified, cylindrical and orange rhizomes. These rhizomes are a modified roots that act as a resistance and storage organs. They grow indefinitely and have excellent regenerative properties.
- Rich in curcuminoids (mainly curcumin), *Curcuma longa* is the most studied plant pharmacologically and has a huge biomedical potential.
- More than 400 pre-clinic assays described and more than 1.000 publications detailing its multiple properties (antioxidant, anti-inflammatory, wound healing, antimicrobial, DNA protecting, etc.)

CAPILIA LONGA™ represents a new activity profile for this species claiming the Phyto-Peptidic Fractions as a new range of bioactives from *Curcuma longa* (Curcumin is only the 2-5% of turmeric powder).

This 100% natural active ingredient is the concentrated secretome of totipotent cells from *Curcuma longa* rhizome. This secretome is rich in signaling peptides specially designed to create the optimal micro-environment to reactivate the hair cycle.

What does turmeric have in common with hair?

Plant tissue

Human hair

- Rooted
- Seasonal behavior (Autumn fall)
- Require nutrients absorption from the surrounding micro-environment
- Presence of a pool of very active Stem cells

Vytrus has found the link:

SIGNALLING PEPTIDES

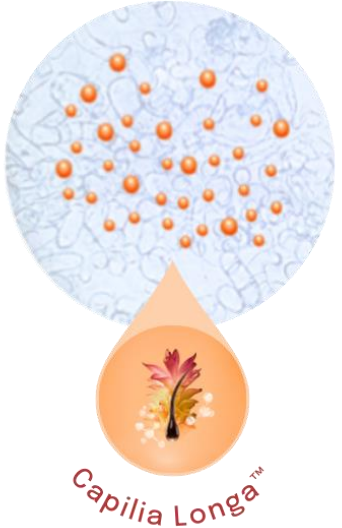
Trough Phyto-Peptidic Fractions technology

The technology: Phyto-Peptidic Fractions

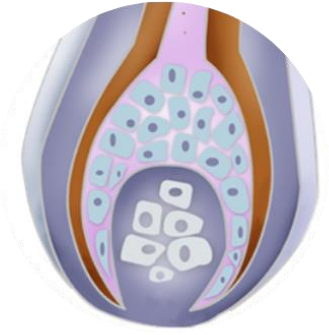
What if we applied plant growth factors to reactivate the hair cycle?

Curcuma Longa

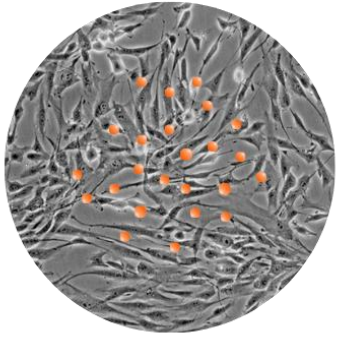
Obtaining the secretome of its stem cells



Applying Capilia Longa™ to the hair system



Reactivated Dermal Papilla



↓ miR-22
↑ IGF-1
↑ miR-31

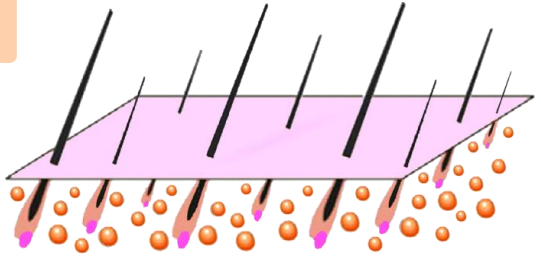
Creating an optimal hair microenvironment

Designed nutritive blend

Oligoelements
(Mg, Fe, Zn, Cu, Ca, etc)

Essential AAs
(Methionine, Cysteine, Proline, etc.)

Vitamins
(C, B1, B2, B3, B5, B6, B8, B9, etc.)



Feeding

Guiding

Concentrated secretome

Phyto-Peptidic Fractions
200kDa, 100KDa, 55kDa, 36kDa,
25KDa, 15kDa, 7KDa
Growth Factors
Transcription Factors
Epigenetic Factors

Biological activity

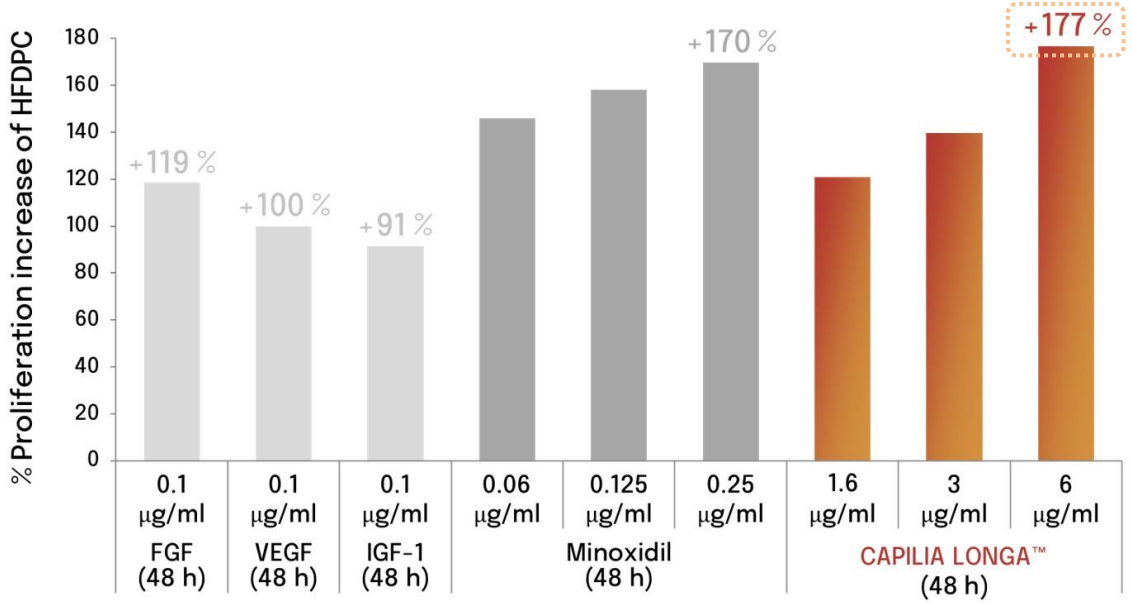
3.1 Induction of Dermal Papilla Cells (HFDPC) Proliferation

3.2 Induction of Insulin Growth Factor-1 (IGF-1) production on HFDPC

3.3 Modulation of miRNA31 and miRNA22 | Expression levels on HFDPC

In vitro efficacy

1. Induction of HFDPC proliferation



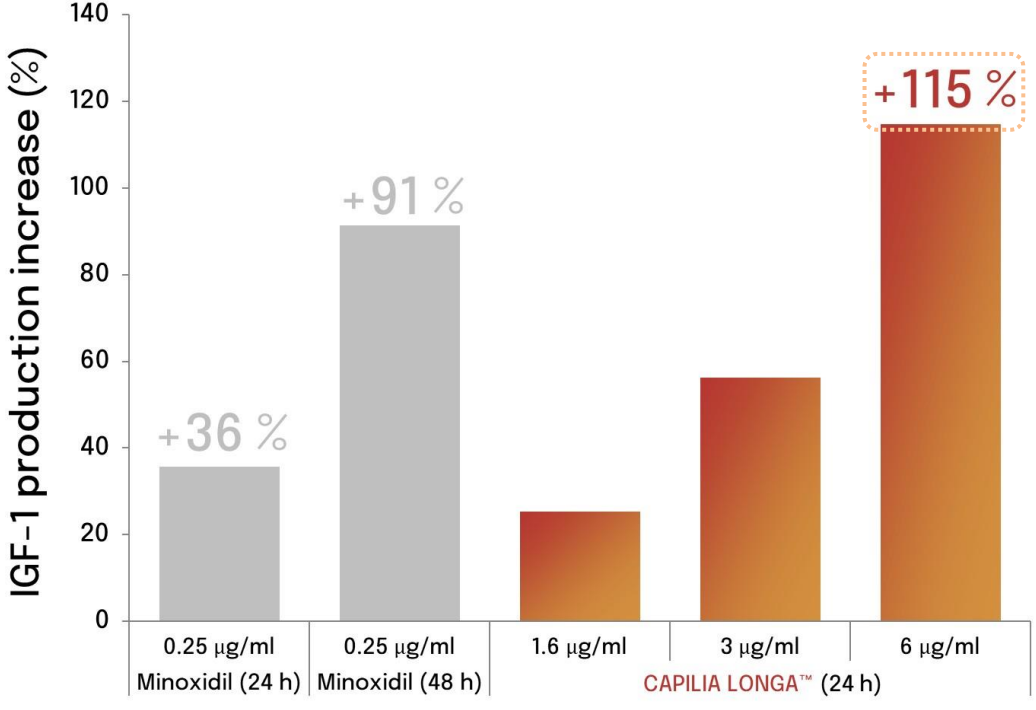
GROWTH FACTOR-LIKE EFFECT

Up to +177% of proliferation increase, showing higher effect than other Growth Factors, and than Minoxidil

Human Follicle Dermal Papilla Cells (HFDPC)
HFDPC were treated with different growth factors, with different concentrations of Minoxidil, or with Capilia Longa™
Cell proliferation was measured by ELISA, measuring the A(450 nm)
% of proliferation increase versus basal levels at 48 h is shown in the graph

In vitro efficacy

2. IGF-1 production increase



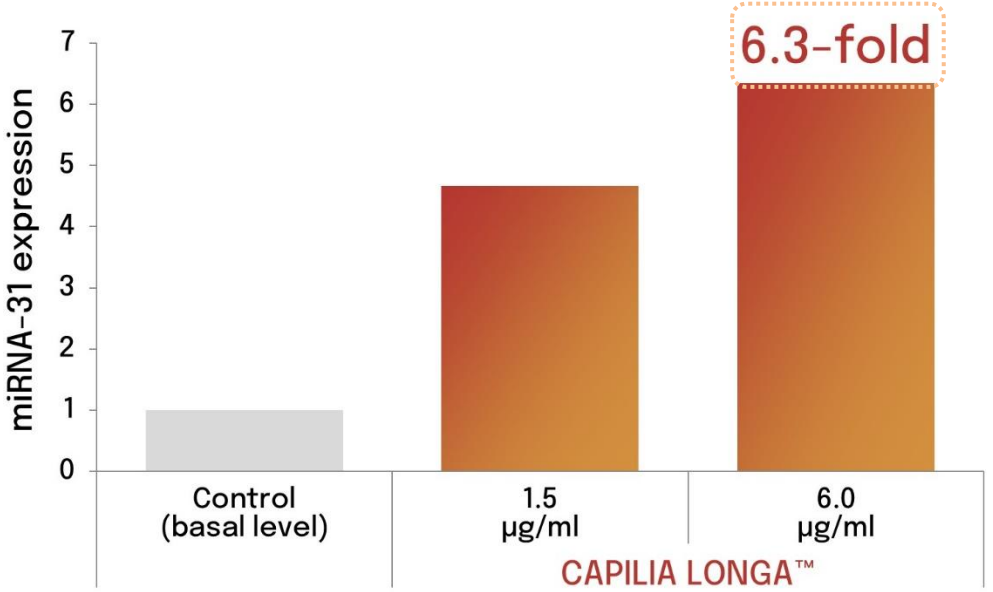
GROWTH FACTOR-LIKE EFFECT

Up to 115% of IGF-1 production increase, showing a faster activity than Minoxidil at 24h

Human Follicle Dermal Papilla Cells (HFDPC)
HFDPC were treated for 24 and 48 h with Minoxidil or with Capilia Longa™
IGF-1 production was measured by ELISA, measuring the A(450 nm)
% of IGF-1 production increase versus basal levels is shown in the graph

In vitro efficacy

3. Modulation of miRNA-31 expression



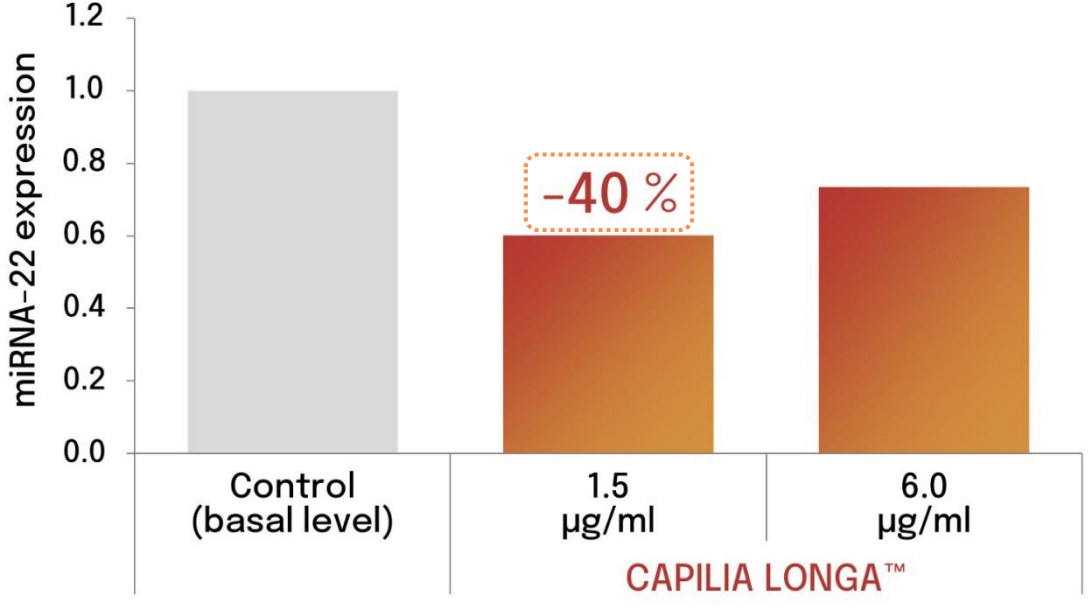
EPIGENETIC STIMULATION OF ANAGEN PHASE

Up to 6.3-fold of miRNA-31 expression stimulation compared to basal levels

Human Follicle Dermal Papilla Cells (HFDPC)
miRNA-31 expression levels determined by qRT-PCR
Basal expression was normalized to 1

In vitro efficacy

3. Modulation of miRNA-22 expression



EPIGENETIC DOWNREGULATION OF CATAGEN & TELOGEN

Up to 40% of miRNA-22 expression reduction compared to basal levels

Human Follicle Dermal Papilla Cells (HFDPC)
miRNA-22 expression levels determined by qRT-PCR
Basal expression was normalized to 1

4. Clinical evaluation

4.1 Anti-Hair Loss efficacy (Combing Test)

4.2 Regenerative efficacy

Global aspect of hair

Hair density increase | Microphotography (TrichoScan®)

4.3 Rebalancing the Hair Cycle (Trichogram)

4.4 Self-Evaluation of volunteers

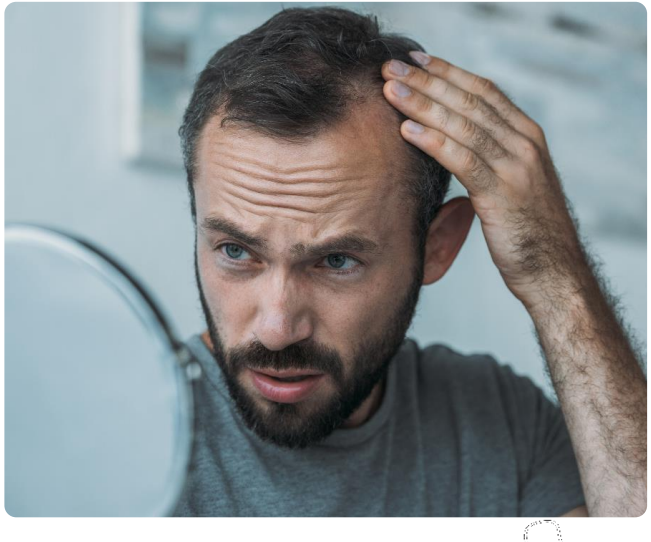
4.5 Eyelash density increase

4.6 Eyebrow density increase

In vivo efficacy 1

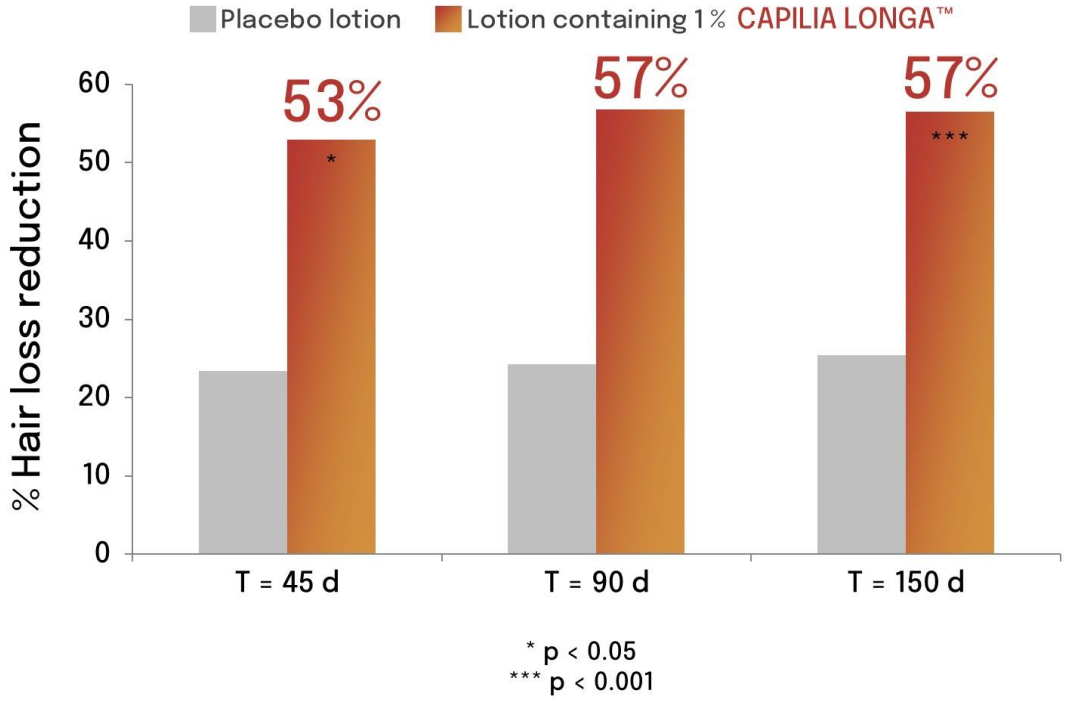
Hair density and reinforcement

- Single blind, placebo-controlled
- Male and Female Androgenetic Alopecia, seasonal alopecia, diffuse alopecia, Hair loss due to menopause.
- A/T<4; **Women** grade Ludwig I-II; **Men** grade Hamilton II-IV.
- 1 application/day on the scalp (by night).



1	%	45 90 150	Days	18-60	Years	40	Volunteers
Dosage							

1. Anti-Hair Loss efficacy | Combing Test



ANTI-HAIR LOSS EFFECT
UP TO 89%

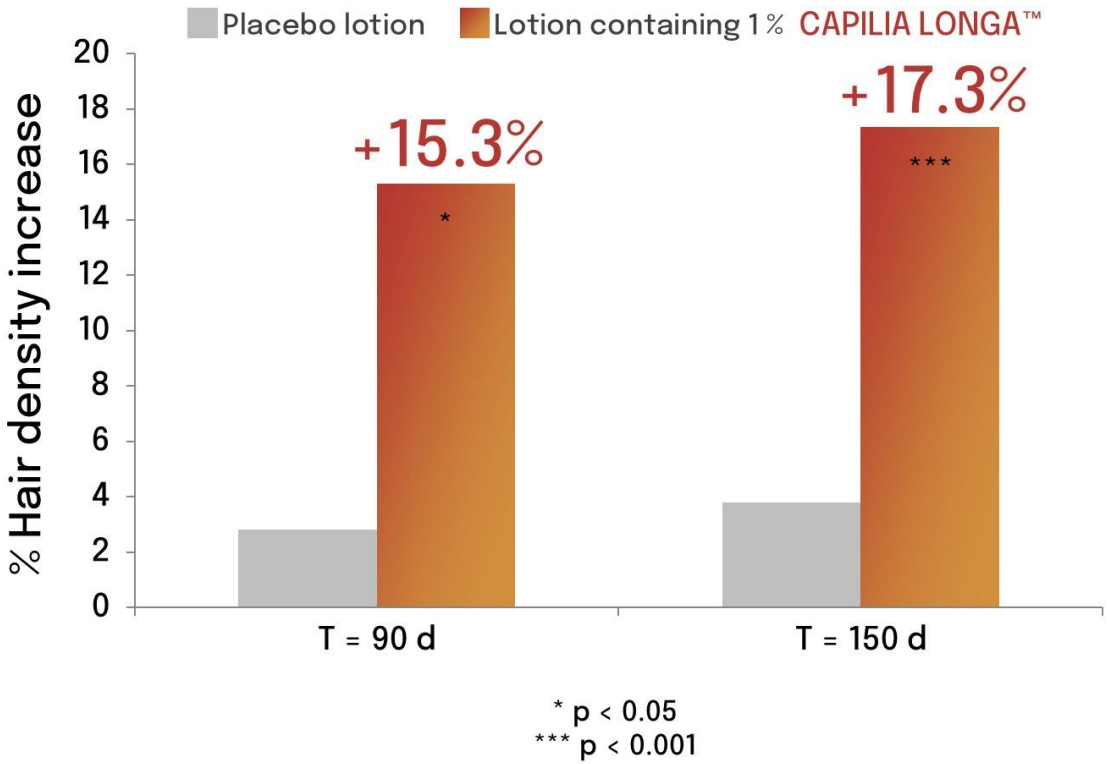
Reduction of hair loss
by 53% at 45 days

2. Regenerative efficacy | Global aspect of hair

Before

After
150 days with
Capilia Longa™

2. Regenerative efficacy | Microphotography (TrichoScan®)

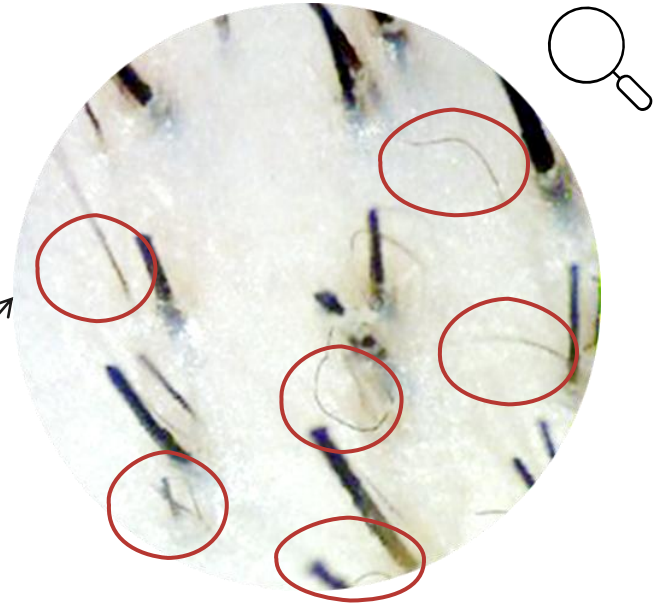


REGENERATIVE EFFECT

Average of 15.3 % and 17.3% of Hair Density increase at 90 & 150 days, respectively

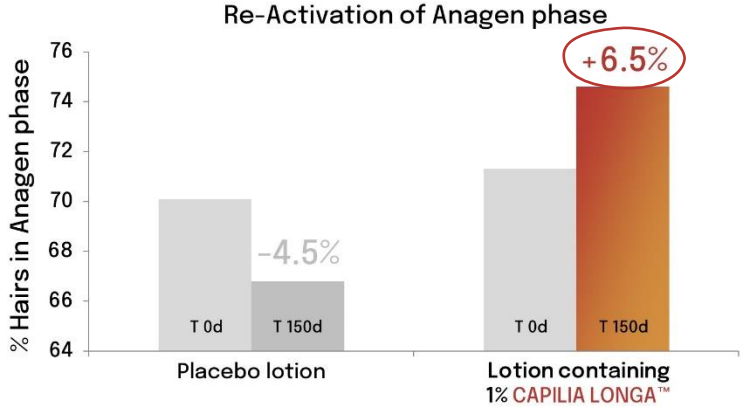
2. Regenerative efficacy | Microphotography (TrichoScan®)

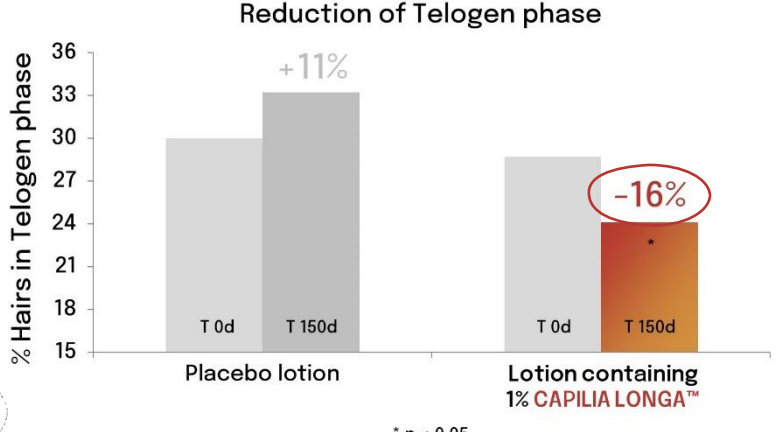
T 0d T 150d

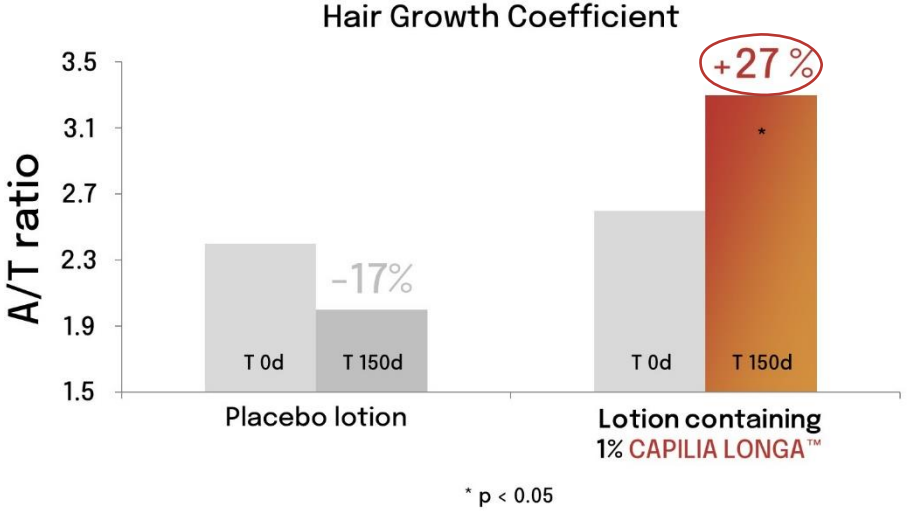


Up to 52% hair density increase at 150d.
13500 new hairs on average

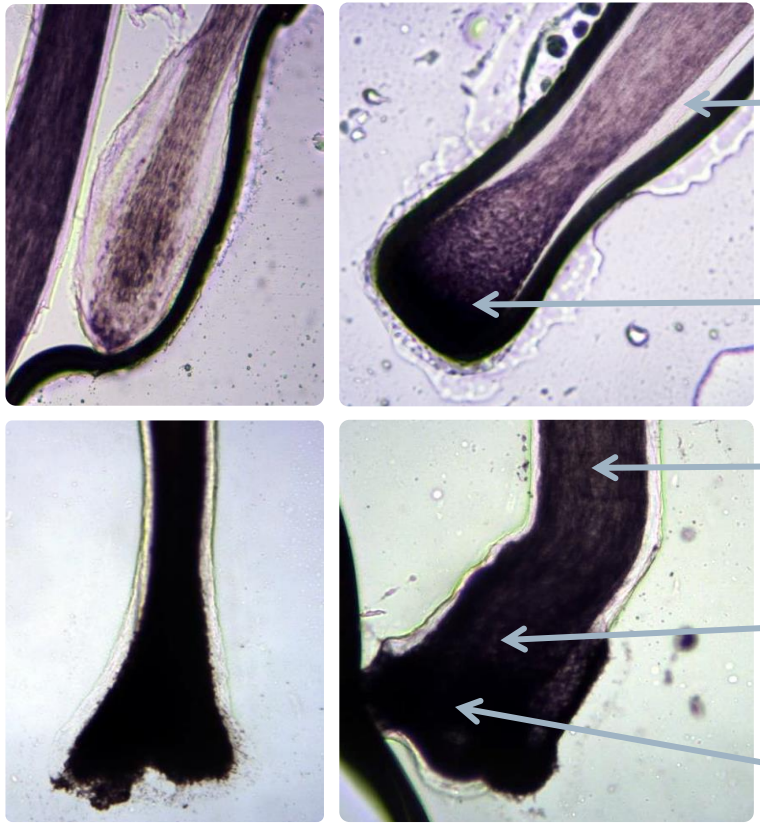
3. Rebalancing the Hair Cycle | Trichogram







3. Rebalancing the Hair Cycle | Trichogram



Well-developed sheaths

Increase of germinative matrix (active keratinocytes)

Thicker hair

Increase of germinative matrix

Broader Bulb

3. Rebalancing the Hair Cycle | Trichogram

- More extensive sheaths
- More developed regenerating area
- Broader and more active bulb
- Better anchored hair

4. Self-Evaluation of volunteers

I notice new hair

85%

Satisfaction rate

75%

Purchase intention

70%

I notice hair loss reduction

95%

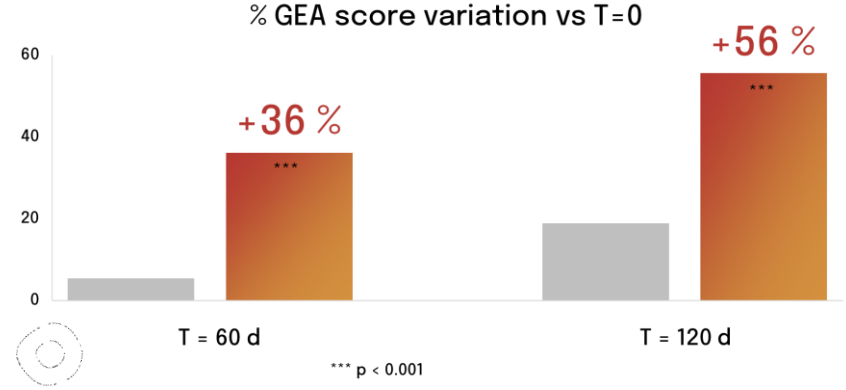
In vivo efficacy 2

Eyebrows and eyelash density

- Female, placebo controlled, halfside face test
- 2 application/day on the brows and lashes.
- Density evaluation by GEA (lash) and GEBA (brow) scale

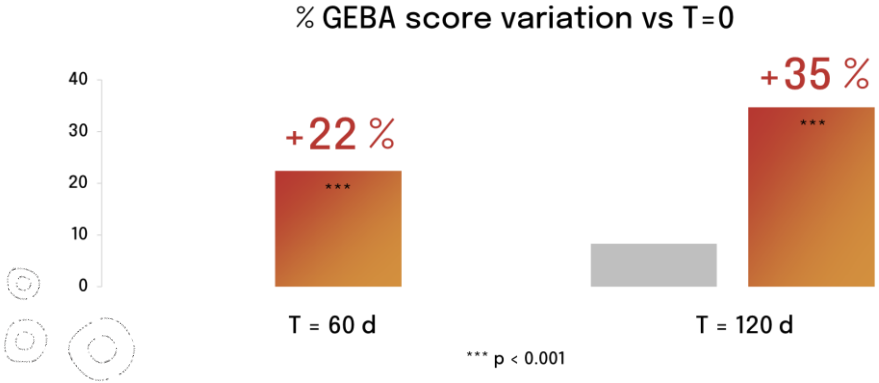
1 %	Dosage	60 120	Days Effect	18–65	Years	20	Volunteers

1. Eyelash density increase



Capilia Longa™ increased the eyelash density up to +200% (3-fold) after 2 and 4 months

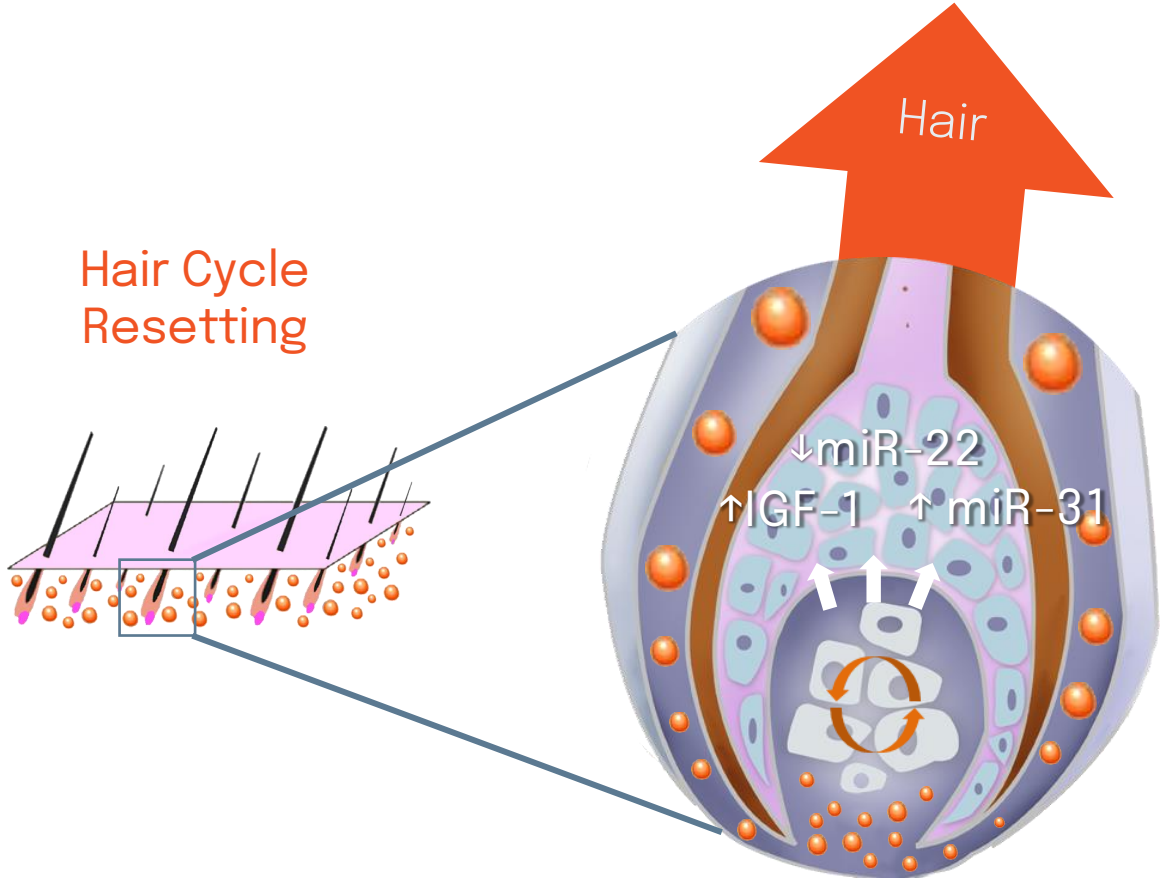
2. Eyebrow density increase



Capilia Longa™ increased the eyebrows density up to +50% (1.5-fold) and +100% (2-fold) after 2 and 4 months

Capilia Longa™ demonstrated...

Hair Cycle Resetting



Creating an optimal microenvironment

Signalling molecules Release

Dermal Papilla Cells Activation

5. Marketing claims and concepts

BOOSTS HAIR DENSITY AND QUALITY

DELAYS HAIR LOSS

EPIGENETIC REBALANCE OF THE HAIR CYCLE

STIMULATES BULB MICROCIRCULATION AND NUTRITION

ACTIVATES THE HAIR FOLLICLE REGENERATION

HAIR CYCLE STIMULATION

6. Applications

PREVENTION AND REDUCTION OF HAIR LOSS PRODUCTS

HAIR STIMULATION AND RE-DENSIFICATION PRODUCTS

BEARD PRODUCTS

HAIR NOURISHING AND STRENGTHENING PRODUCTS

TREATMENTS FOR FRAGILE/WEAK/LACKING VOLUME HAIR TYPES

EYELASH AND EYEBROW ENHANCING PRODUCTS

7. Technical information

Technical information

Declarations

Free from: GMO, BSE, gluten, palm oil, cosmetic allergens*, nanomaterials, VOC

COSMOS approved

ISO 16128 Natural Origin Index: 100%

INCI

Curcuma Longa (Turmeric) Root Extract, Water (Aqua), Pentylene Glycol, Phytic Acid

Dosage

Suggested use level: 0.5 – 2%

Formulation

Water and ethanol soluble.

Incorporation during the cooling phase (<40°C).

*In accordance with Regulation (EC) No. 1223/2009, Annex III, No. 67-92

vytrus biotech

Natural Innovation for a Better Life

www.vytrus.com