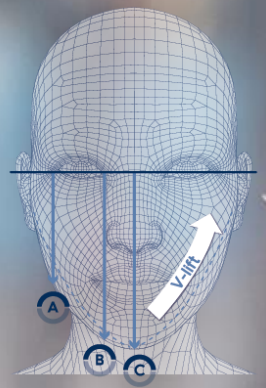
LIPOTRUE
science & biotechnologies

SIRTALICE™

A FREEZING BLAST FROM THE DEEP SEA



V-lift in
30 min!

v. 0

SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

Marine bio-research, more than water

- **Ocean**, lifeblood of Earth, has an untapped potential, with **only a 5% explored**
- **Unique species** from the ocean's depths and sea breeze, to the marine cnidarians and onshore halophyte plants
- In collaboration with **research institutes**, we have **proprietary collections** of microorganisms for an **unlimited source** of **new active ingredients**

Over 22,000 microorganisms at our disposal


Malaspina Expedition


Mediterranean Expedition


Marine cnidarian


Halophyte Plants*


Extreme aquatic environments

…and more True novel active ingredients yet to be unveiled

LIPOTRUE
science & biotechnologies

* Courtesy of IMEDEA: Arthrocnemum project, 2015

Malaspina expedition, inspired by history

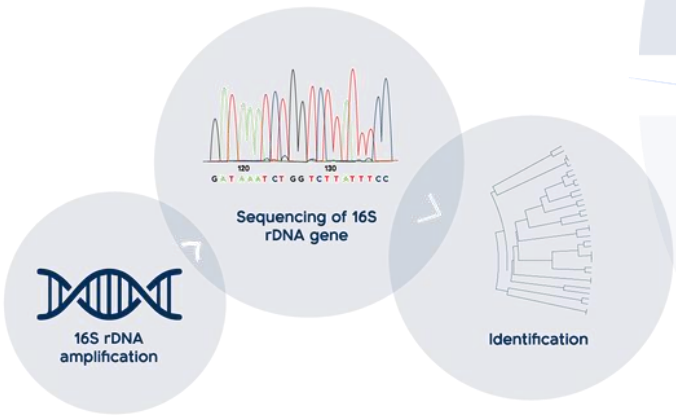
Inspired in the first expedition in **1789**, a **oceanographic research** vessel set sail in a a journey around the world

- ≥ **42,000 nautical miles** of international waters navigated
- Over **350 marine water samples** collected
- Over **120 unknown bacterial** strains isolated
- Different **depths, temperatures, salinities** and **oxygen** levels

Courtesy of CSIC: Malaspina expedition, 2010

Strain classification and identification

- Classification and identification of isolated microorganisms by **MALDI-TOF MS** in a HTS analysis and **16S ribosomal RNA** sequencing
- **Cultured** (only 1% of the population) and **new uncultured species**
- **Evaluation** and **characterization** of derived extracts through metabolomics and other techniques



Phylogenetic tree of bacterial strains

SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

Transforming it into Smart Data

- **Derived extracts efficacies** are analyzed through **transcriptomics** generating a great amount of data
- **Smart data** for the development of new active ingredients with **outstanding efficacies**
- Two strategies:
  - ➢ Identify the **mechanism of action** of an active ingredient
  - ➢ Define the **best active ingredient** for a **specific** mechanism of action

LIPOTRUE
science & biotechnologies

Sirtalice™, a freezing blast from the deep sea

Sirtalice™, is an active marine ingredient from a microorganism collected during the **Malaspina** expedition, near **Reunion Island** (Indian ocean)

Coral barriers form shallow lagoons **of turquoise waters** that shelter thousands of marine species

61° 24' 42'' E
30° 03' 30'' S

The microorganism was collected at:

Depth: 3,400 m

Temperature: 1.5 °C

Oxygen level: 3.8 µmol/L

Sirtalice™, a freezing blast from the deep sea

An on-the-go freezing blast **to help breath out your *true* beauty**, offering an **instant lifting** and a **V-reshape** of face contour

- **Recharges your skin**, boosting **cellular energy and skin contraction** (*in vitro* and on human skin explants)
- **Reinforces skin cohesion**, enhancing **focal adhesions** (*in vitro*, on human skin explants, and *in vivo*)
- **Instant lifting & V-shape** effect with long-lasting efficacy (*in vivo*)

SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

Your skin needs a quick charge

- Time is precious in current fast-changing societies, but **skin is a treasure** that needs time to be **cared for**

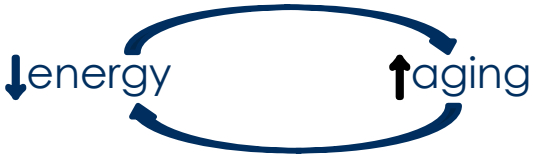
- Your skin deserves an **on-the-go recharging quick fix** to keep up with your daily rhythm

A refreshing wind for always being selfie- ready

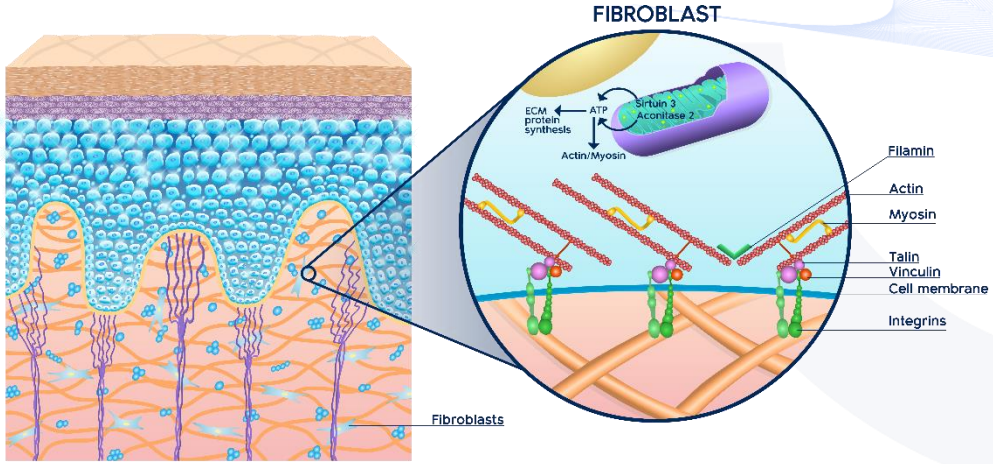
LIPOTRUE
science & biotechnologies

Mitochondria are the skin inner chargers

Skin needs energy to cope with environmental stressors and to repair its damage



- Mitochondria generate energy during **mitochondrial respiration**



- A difference in electrical charge on either sides of the mitochondrial membrane

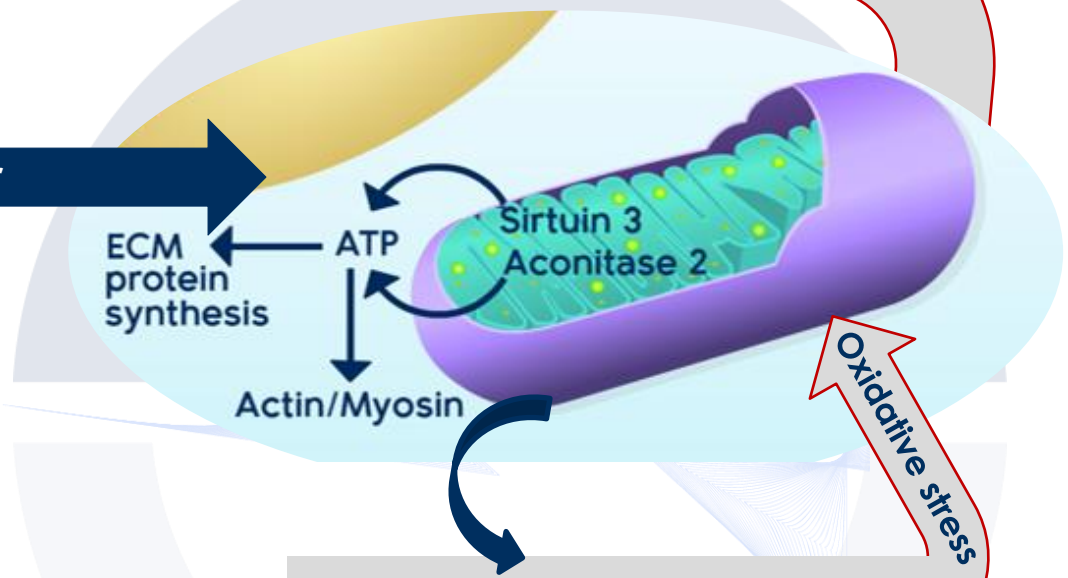
ATP

Mitochondrial aerobic respiration

- Aerobic mitochondrial respiration
  - ➢ Uses oxygen in tissues

mtDNA damage leads to mitochondrial respiration dysfunction: ↑**ROS** ↓**ATP**

Main ATP supplier



Oxidative stress

➢ **ROS** generator as by-products of **impaired respiration**

Removed

✓ Efficiently by **antioxidants** and free radical scavenging enzymes

↑ **Matrix Metalloproteases (MMPs)**

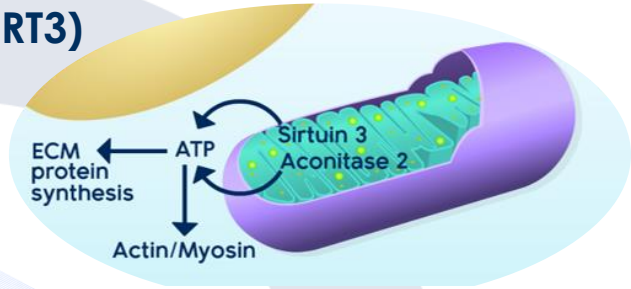
↑ **ECM proteins degradation**

SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

A recharging longevity

Oxidative stress is key for **longevity**

- **Longevity** associated maintenance protein **Sirtuin 3 (SIRT3)**



  - ➢ **Controls ATP synthesis** through TCA cycle (Krebs)
  - ➢ **Increases antioxidant** activity (eg. SOD2, GSH)

✓ **Modulation of ROS production and scavenging**

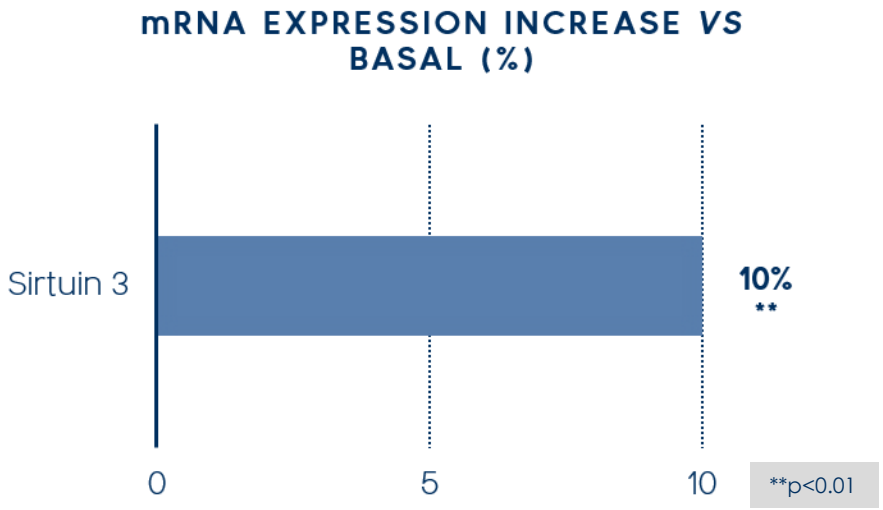
Genetic association between SIRT3 and longevity

LIPOTRUE
science & biotechnologies

In vitro efficacy: transcriptomics by Dermoarray (fluorescence)

- Primary human epidermal fibroblasts
- 0.05 mg/mL **Sirtalice™ active ingredient***
- 24 h incubation
- 600 genes expressed in skin cells

✓ **Up-regulation** of **sirtuin 3** gene, which may **enhance cellular energy** while **protecting** mitochondria from the oxidative stress, hence, **improving longevity**



➢ Microarrays can be used to study the extent to which certain genes are turned on or off in cells and tissues

LIPOTRUE science & biotechnologies

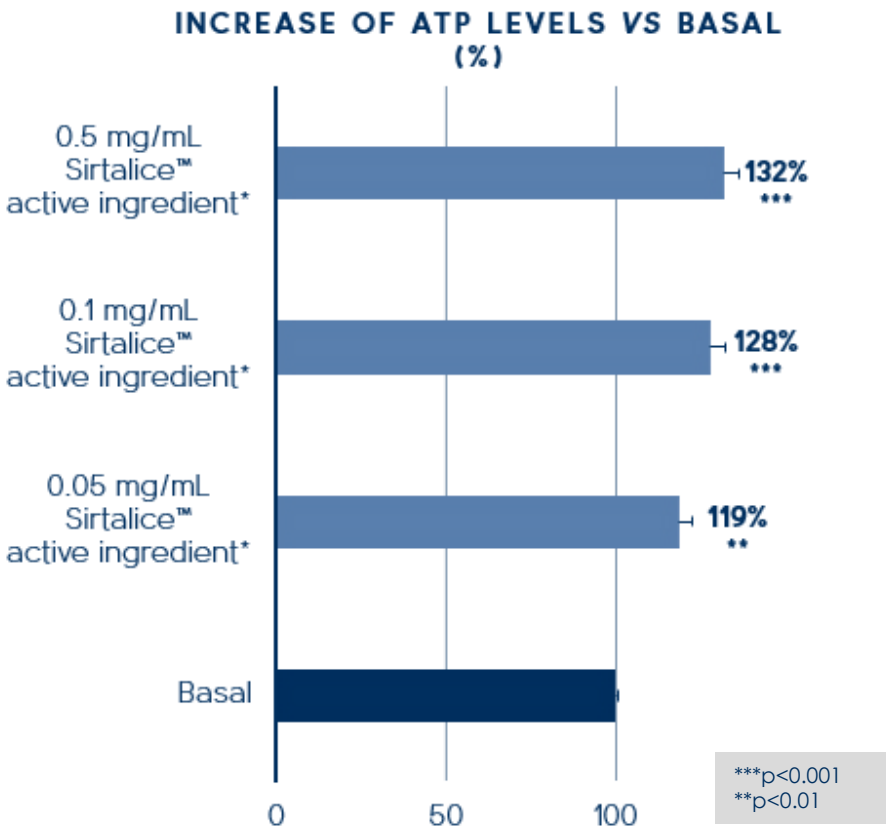
*This test has been performed without solvents nor preservatives

***In vitro efficacy*: recharging skin cells** (luminescence)

- Normal human dermal fibroblasts
- 3 h incubation with low-glucose medium (↓ ATP)
- 30 min incubation

✓ **32% ATP** increase with 0.5 mg/mL *vs* non-treated cells, which may imply a **recharging of energy skin cells breaking the skin aging feedback loop**

✓ **Dose-dependent efficacy**



LIPOTRUE science & biotechnologies

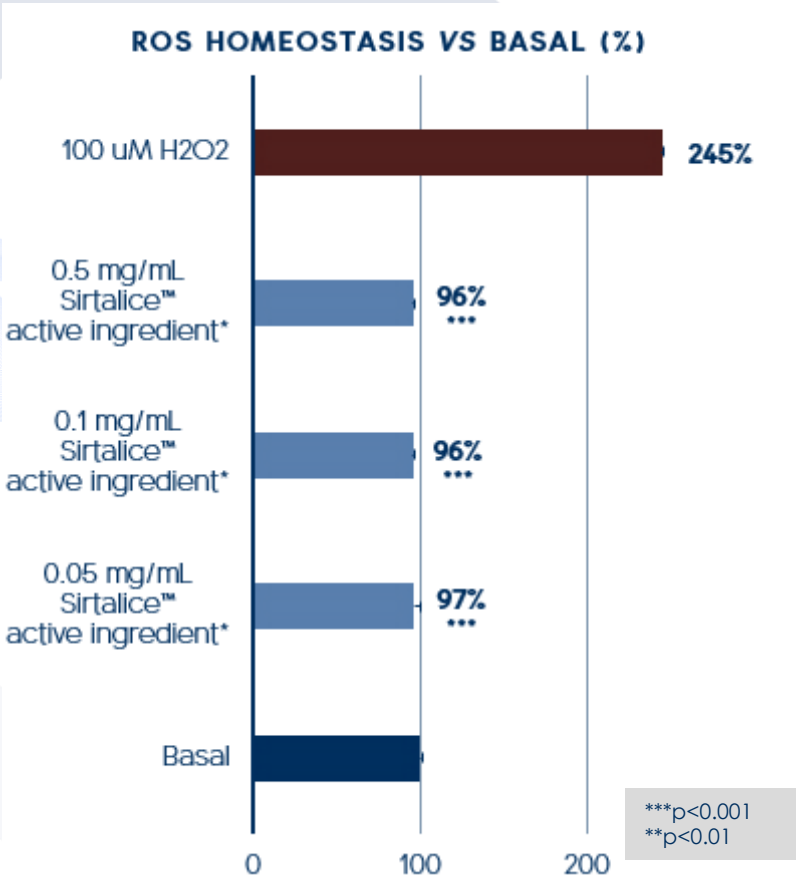
*This test has been performed without solvents nor preservatives

In vitro efficacy: oxidative damage under control
(fluorescence)

- Primary human dermal fibroblasts
- 24 h incubation

✓ **4% less ROS** with 0.5 mg/mL *vs* non-treated cells, **maintaining oxidative homeostasis** although inducing ATP levels

✓ **Energy boosting keeping oxidative species under control**



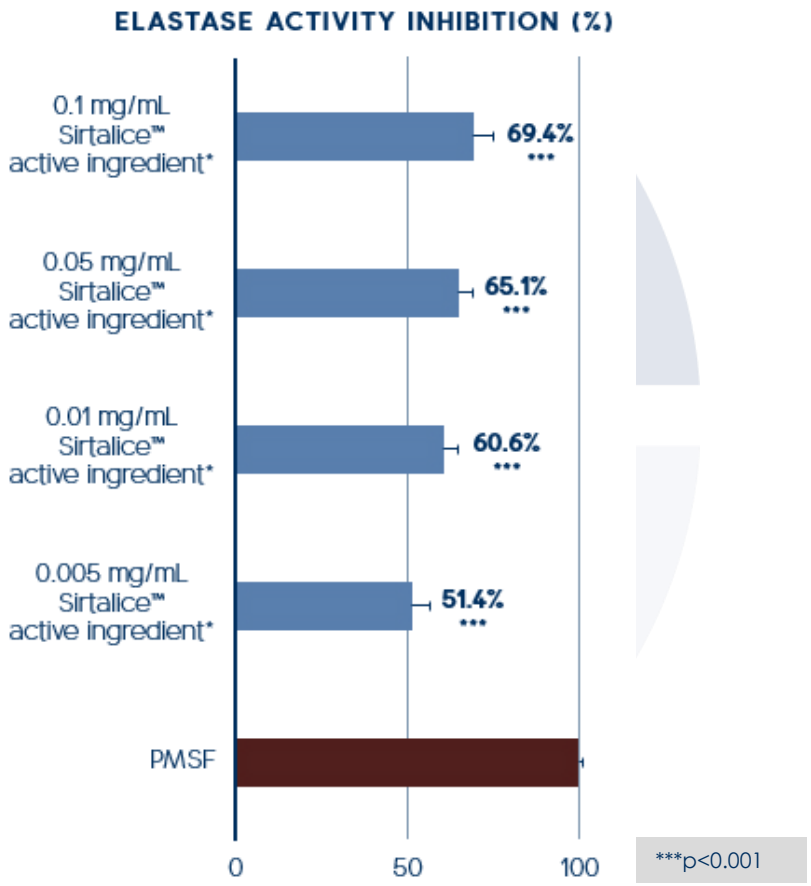
LIPOTRUE science & biotechnologies

*This test has been performed without solvents nor preservatives

***In vitro efficacy*: protection of ECM proteins**
(enzymatic)

- Positive control: Phenylmethanesulfonyl fluoride (PMSF)
- Absorbance (405 nm)

✓ **69% elastase inhibition** with 0.1 mg/mL, **preventing enzymatic degradation of ECM proteins**



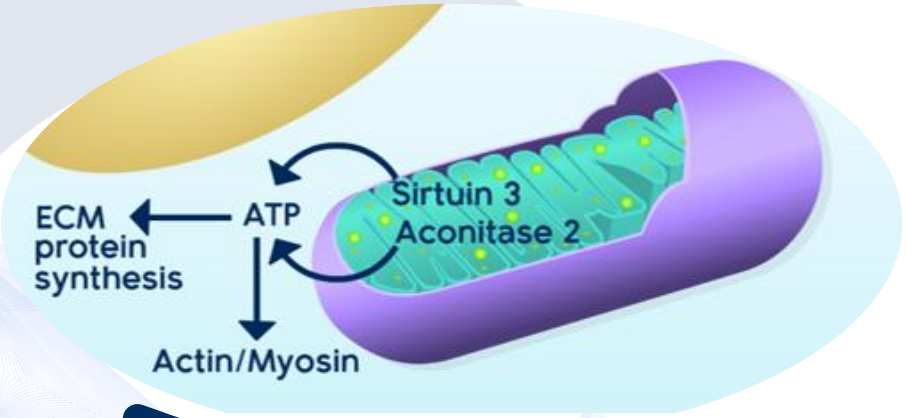
*This test has been performed without solvents nor preservatives

Moonlighting charge and oxidative protection

Mitochondrial aconitase is a **moonlighting enzyme**

- **Controls mitochondrial ATP production**
  - Catalyzes the second step of the TCA cycle

High-energy electrons



- **Stabilizes mtDNA**
  - Encodes proteins of mitochondrial respiration

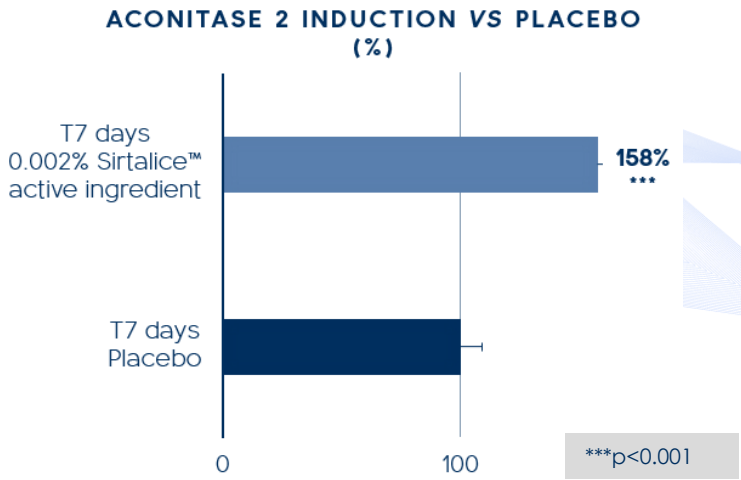
↑ATP ↓ROS

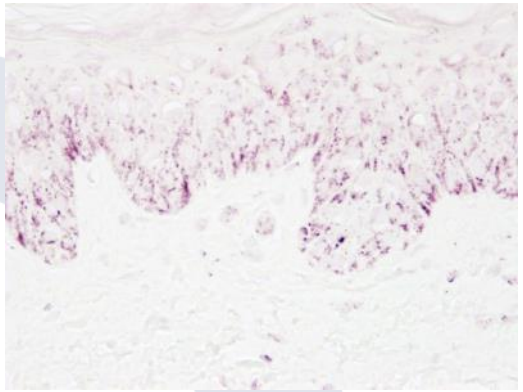
- Moonlighting proteins have an enzymatic function and have acquired another non-enzymatic activities through evolution

SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

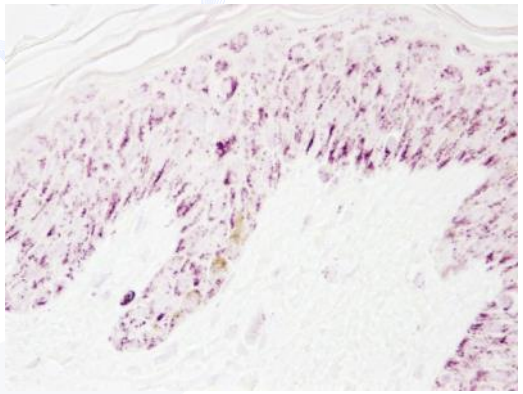
***Human skin explants efficacy*: inducing and stabilizing mitochondrial respiration**

- Human skin explants (65-year old woman donor), immunostaining
- 7 days
- Cream with 0.002% Sirtalice™ active ingredient





T7 days Placebo



T7 days 0.002% Sirtalice™ active ingredient

✓ **58% aconitase 2** increase vs placebo, helping to **stimulate mitochondrial respiration** and, hence, cellular **energy**

✓ **Moonlighting** enzyme induction that would **stabilize and protect mtDNA from oxidative stress**

LIPOTRUE
science & biotechnologies

SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

Energy also for skin contraction

Cells need energy to cope with mechanical forces and maintain their shape and connections to ECM and other cells

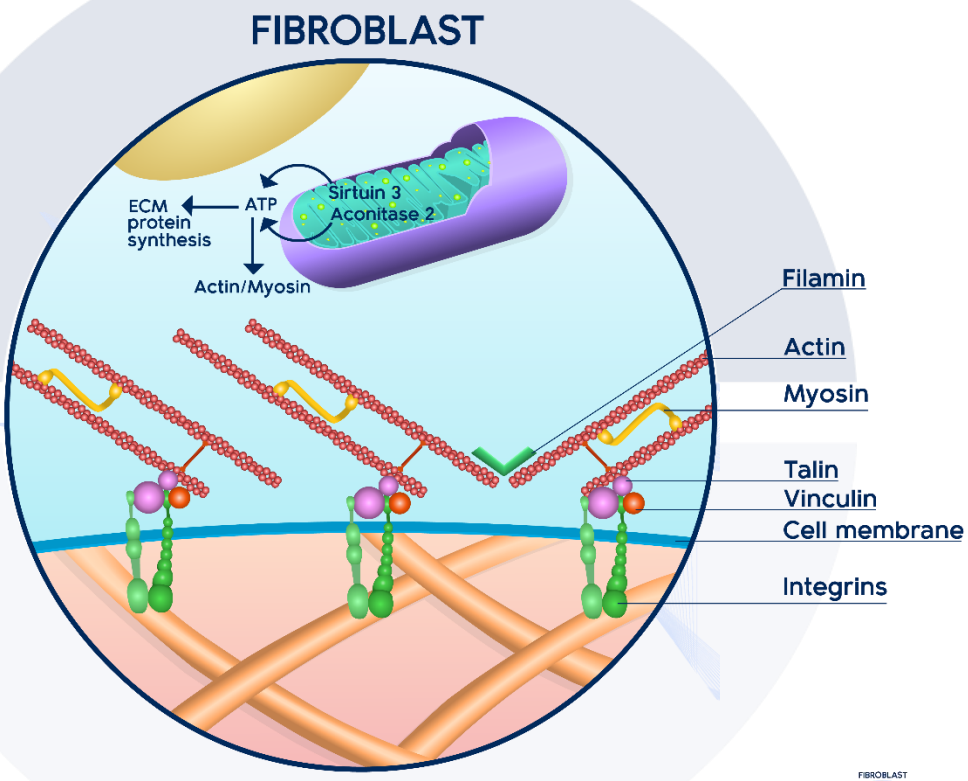
- Myosin uses ATP to cross-link **actin filaments** (**stress fibers**)

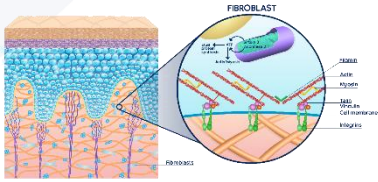
✓ **Connect to focal adhesions (talin, vinculin)**

✓ **Integrin reinforcement**

Collagen I expression stimulation

Stronger adhesion to ECM (pulling)





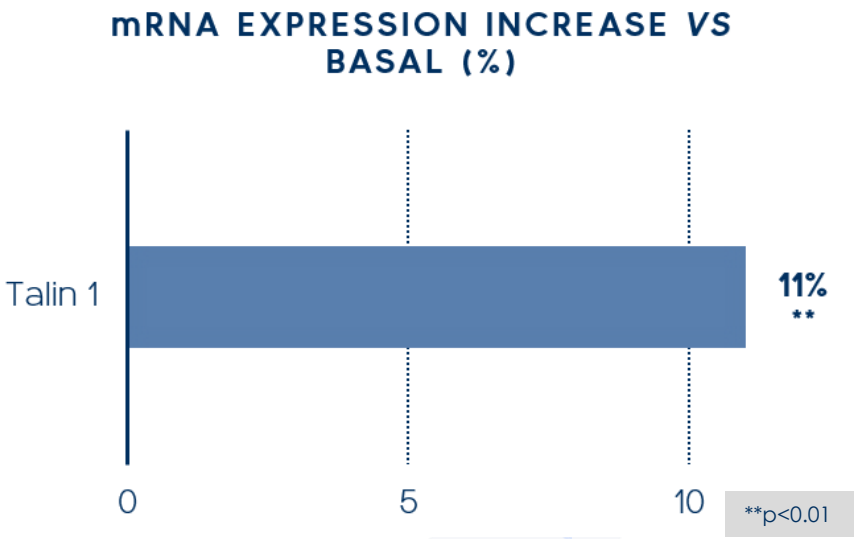
LIPOTRUE
science & biotechnologies

In vitro efficacy: transcriptomics by Dermoarray (fluorescence)

- Primary human epidermal fibroblasts
- 0.05 mg/mL **Sirtalice™ active ingredient***
- 24 h incubation
- 600 genes expressed in skin cells

✓ **Up-regulation** of **talin 1** gene, which may be linked to an increase of actin-myosin crosslinking due to ATP induction

✓ Enhancement of **focal adhesion protein genes**

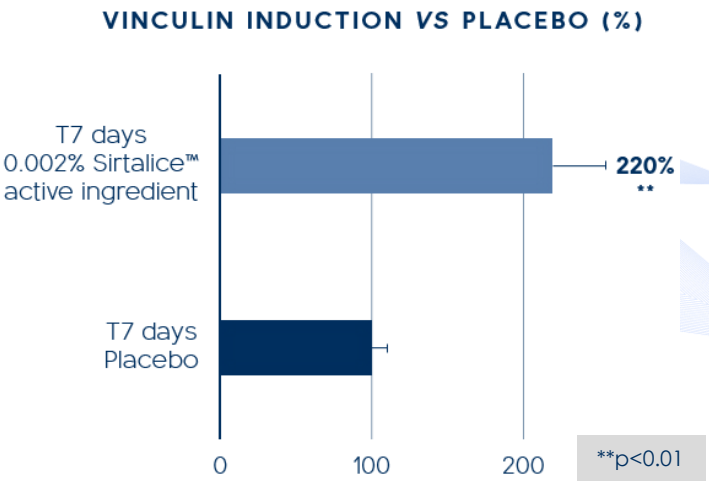


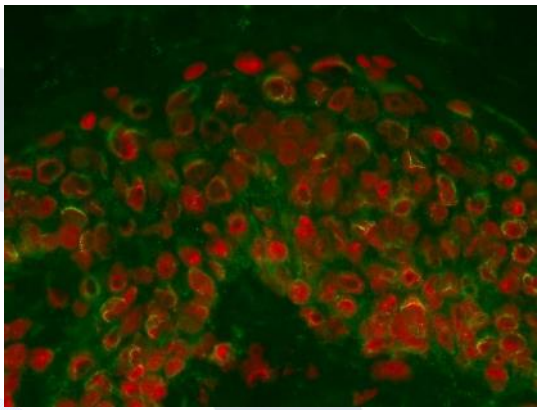
➢ Microarrays can be used to study the extent to which certain genes are turned on or off in cells and tissues

*This test has been performed without solvents nor preservatives

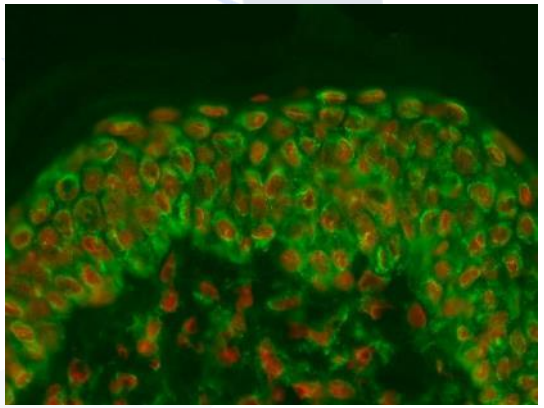
***Human skin explants efficacy*: reinforcement of focal adhesions**

- Human skin explants (65-year old woman donor), immunostaining
- 7 days
- Cream with 0.002% Sirtalice™ active ingredient





T7 days
Placebo



T7 days
0.002% Sirtalice™
active ingredient

✓ **120% vinculin** increase *vs* placebo, helping to **strengthen focal adhesions**

✓ Reinforcing cell adhesions to ECM, could imply a **pulling effect of ECM network** due to actomyosin contraction

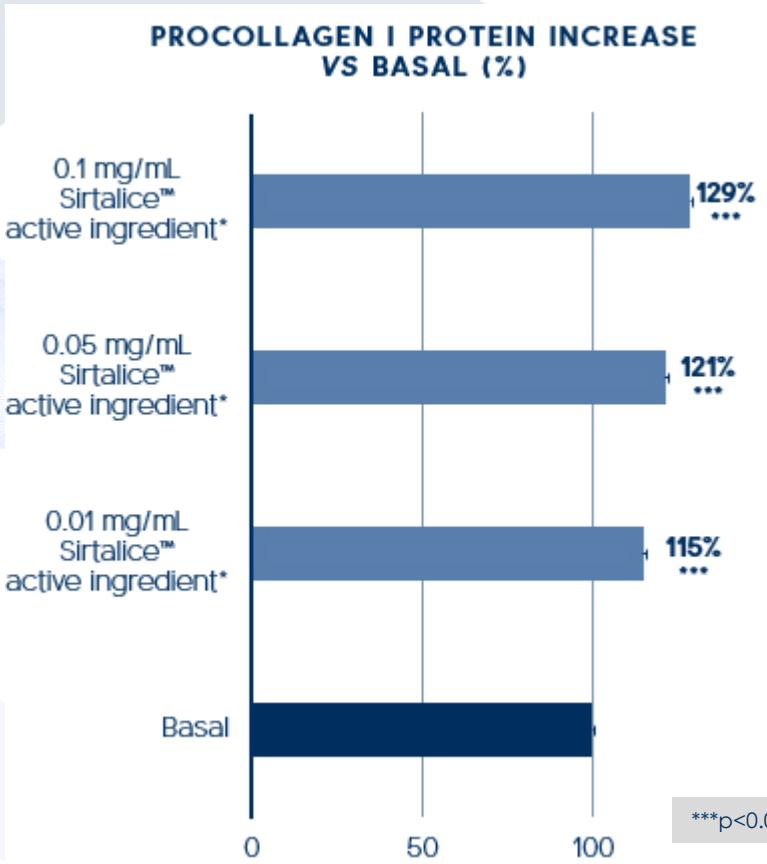
SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

***In vitro efficacy*: collagen boosting** (ELISA)

- Normal human dermal fibroblasts
- 48 h incubation

✓ **29% procollagen I induction** with 0.1 mg/mL *vs* non-treated cells, which could have been induced by focal adhesions reinforcement

✓ Enhancement of skin structural integrity for a **firming effect**



LIPOTRUE science & biotechnologies

*This test has been performed without solvents nor preservatives

In vivo efficacy: tightening flash efficacy

20 Caucasian women (35-45 years old) applied a cream with **2% Sirtalice™** on half face, twice daily for 28 days. A placebo was applied on the other half of the face

Evaluation of:

- Elasticity & firmness (**Cutometer®**)
- Lifting effect (**morphometric image**)
- Wrinkles & smoothness (**fringe projection**)
- Radiance & hydration(**Colorimeter, Corneometer®**)

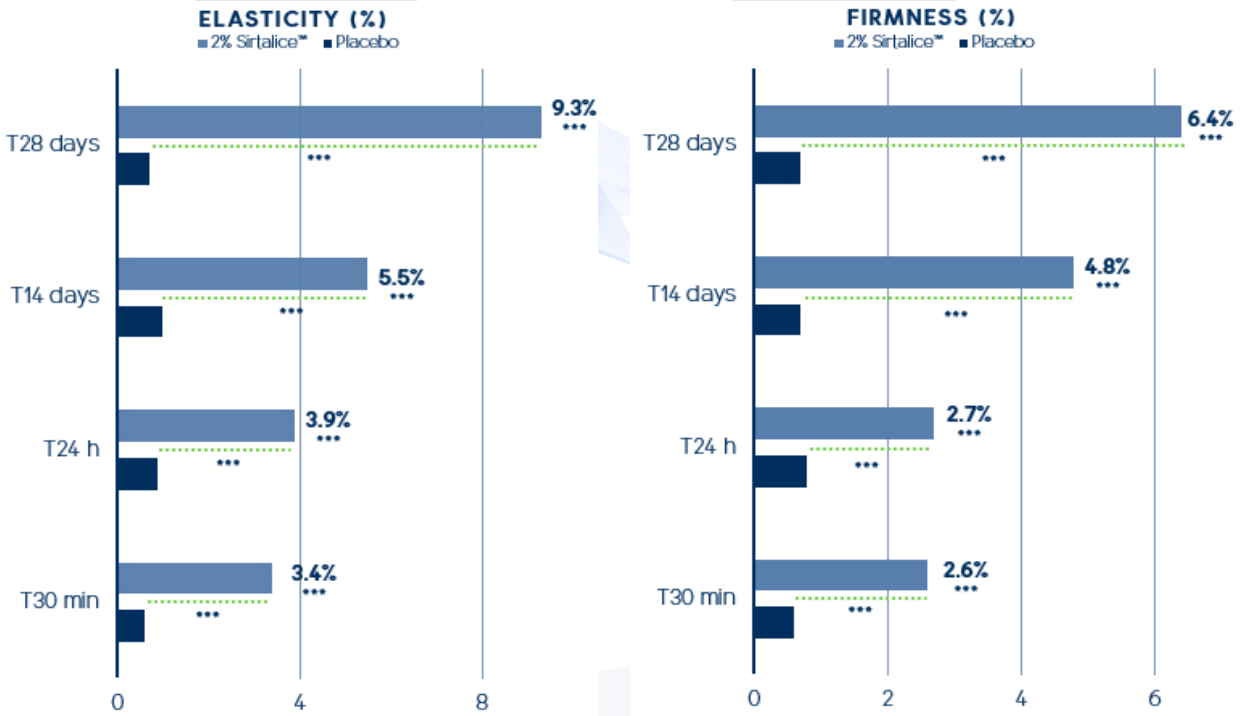
SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

In vivo efficacy: tightening flash efficacy

- Elasticity & firmness (Cutometer®)
- Cream with 2% Sirtalice™ *vs* placebo
- Half face, 28 days, twice daily
- Age: 35-45

✓3% elasticity and firmness increase in 30 min

✓Up to 13.3% and 11.4% more elastic and firmer skin after one month, respectively



***p<0.001
***p<0.001 *vs* placebo

LIPOTRUE
science & biotechnologies

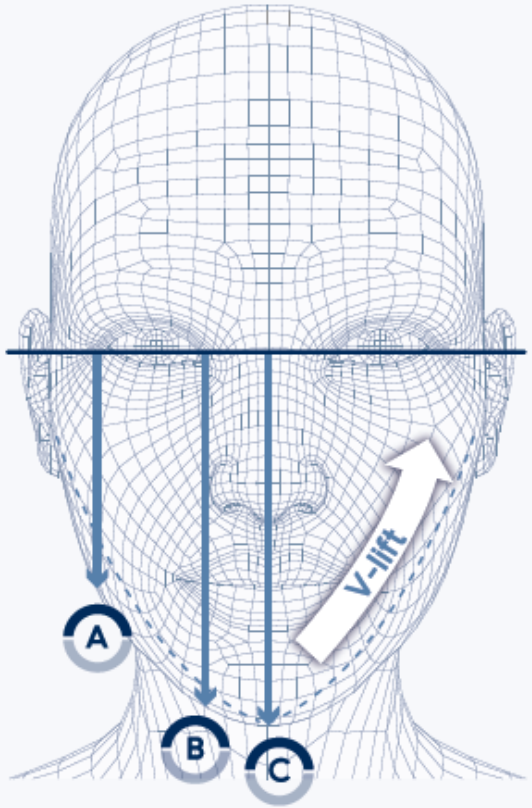
In vivo efficacy: tightening flash efficacy

- Lifting effect (morphometric image)
- Cream with 2% Sirtalice™ *vs* placebo
- Half face, 28 days, twice daily
- Age: 35-45

✓ **Lifting effect after 30 min**

✓ **V-reshape of face contours with time**

	T30 min	T28 days
A	-2.17 mm	-2.19 mm
B	-1.44 mm	-2.56 mm
C	-0.96 mm	-0.80 mm



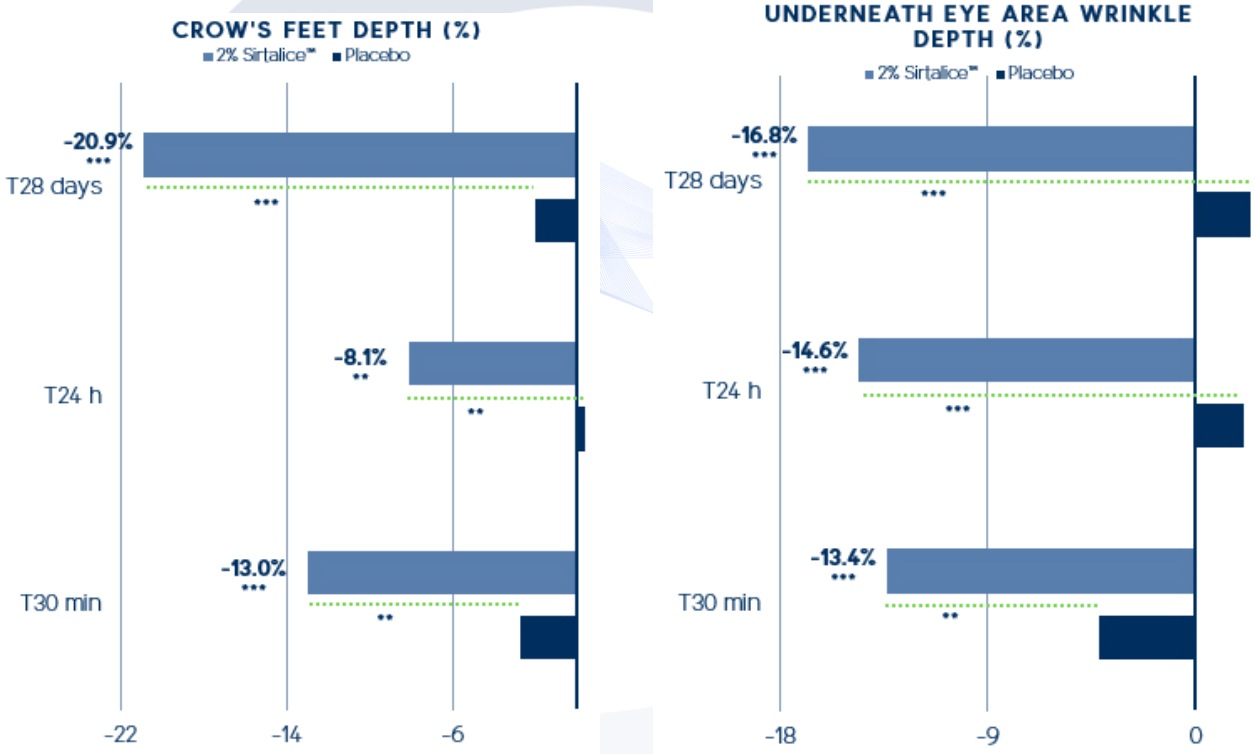
SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

In vivo efficacy: tightening flash efficacy

- Wrinkles & smoothness (fringe projection)
- Cream with 2% Sirtalice™ *vs* placebo
- Half face, 28 days, twice daily
- Age: 35-45

✓ **13% wrinkle depth reduction in only 30 minutes**

✓ **Up to 34% and 33% improvement in crow's feet and underneath eye in only 30 minutes**



***p<0.001
**p<0.01
***p<0.001 *vs* placebo
**p<0.01 *vs* placebo

LIPOTRUE
science & biotechnologies

SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

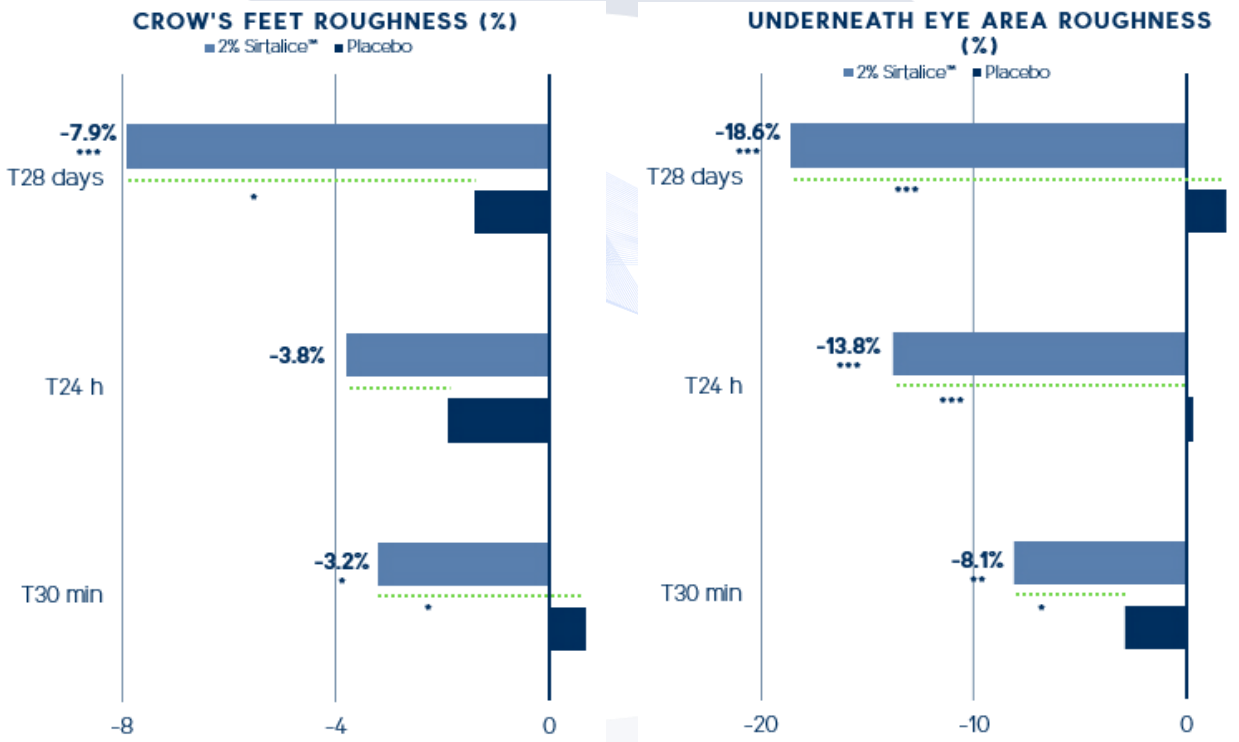
***In vivo efficacy*: tightening flash efficacy**

- Wrinkles & smoothness (fringe projection)
- Cream with 2% Sirtalice™ *vs* placebo
- Half face, 28 days, twice daily
- Age: 35-45

✓ 3% and 8% wrinkle smoothness in only 30 minutes in crow's feet and underneath eyes, respectively

✓ Up to 26% and 25% efficacy in 30 minutes

✓ Up to 44% improvement in underneath eyes in one month



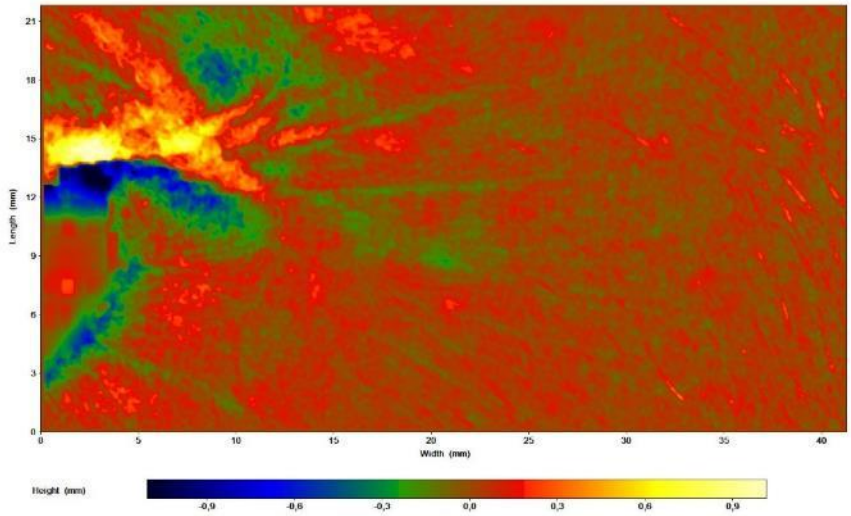
***p<0.001
**p<0.01
*p<0.05
***p<0.001 *vs* placebo
*p<0.05 *vs* placebo

LIPOTRUE
science & biotechnologies

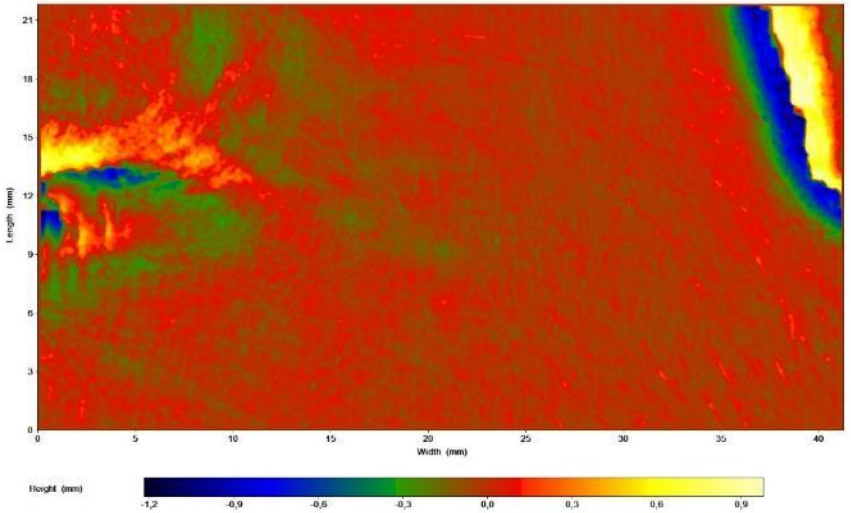
In vivo efficacy: tightening flash efficacy

- Wrinkles & smoothness (fringe projection)
- Cream with 2% Sirtalice™ *vs* placebo
- Half face, 28 days, twice daily
- Age: 37 (volunteer 15)

T0 days



T28 days



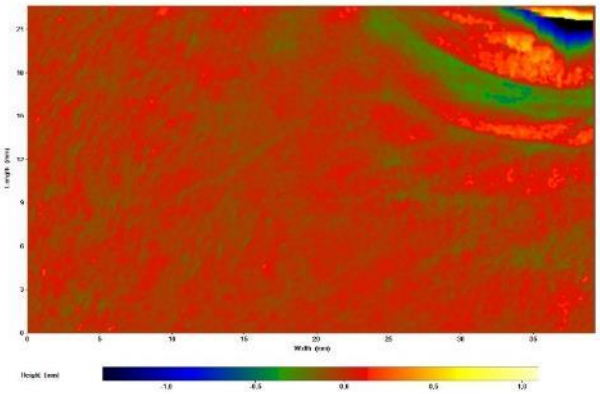
Crow's feet depth: ↓24.6%
Crow's feet roughness: ↓6.8%

SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

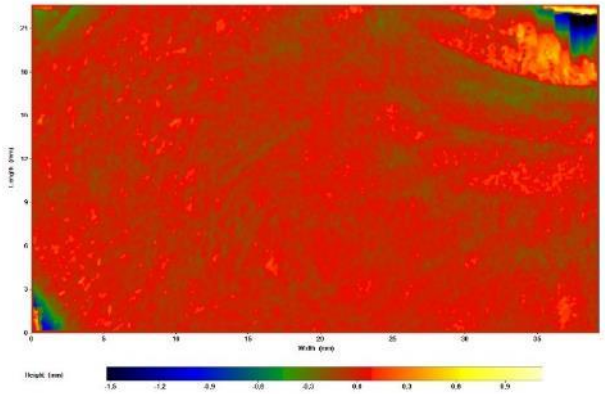
In vivo efficacy: tightening flash efficacy

- Wrinkles & smoothness (fringe projection)
- Cream with 2% Sirtalice™ *vs* placebo
- Half face, 28 days, twice daily
- Age: 43 (volunteer 10)

T0 days

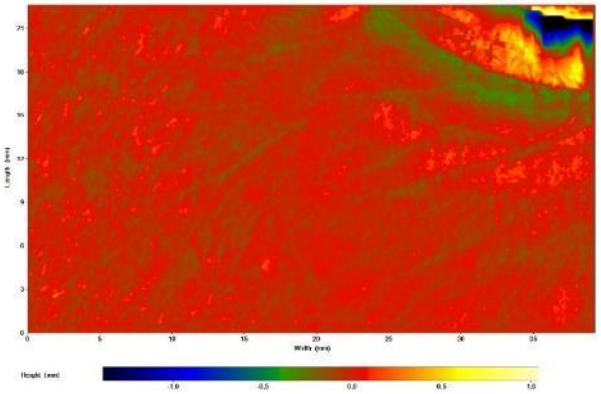


T30 min



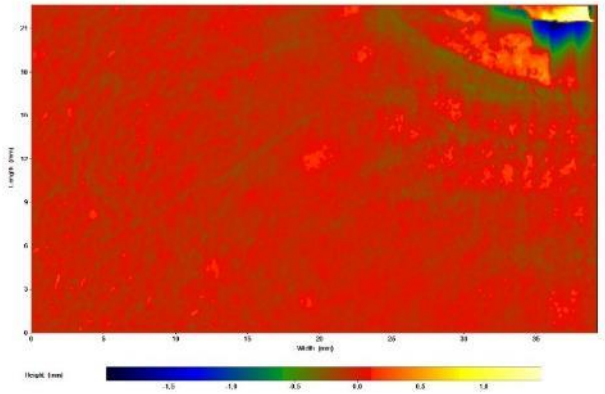
Crow's feet depth: ↓22.3%
Underneath eye wrinkle depth: ↓32.6%

T24 h



Crow's feet depth: ↓27.5%
Underneath eye wrinkle depth: ↓33.1%

T28 days



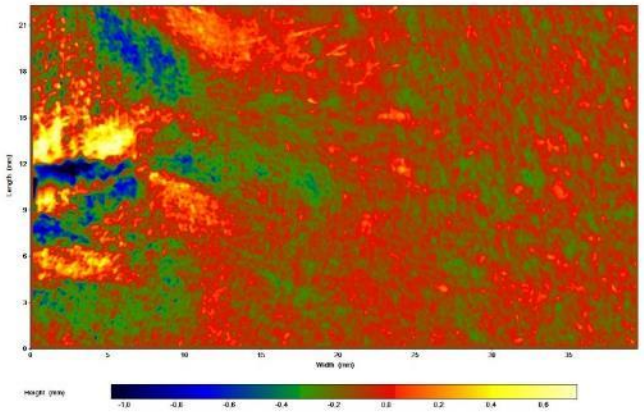
Crow's feet depth: ↓23.9%
Underneath eye wrinkle depth: ↓33.9%

LIPOTRUE
science & biotechnologies

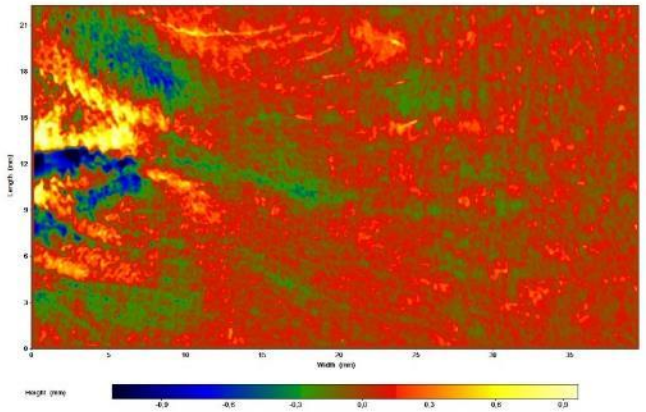
In vivo efficacy: tightening flash efficacy

- Wrinkles & smoothness (fringe projection)
- Cream with 2% Sirtalice™ *vs* placebo
- Half face, 28 days, twice daily
- Age: 45 (volunteer 18)

T0 days



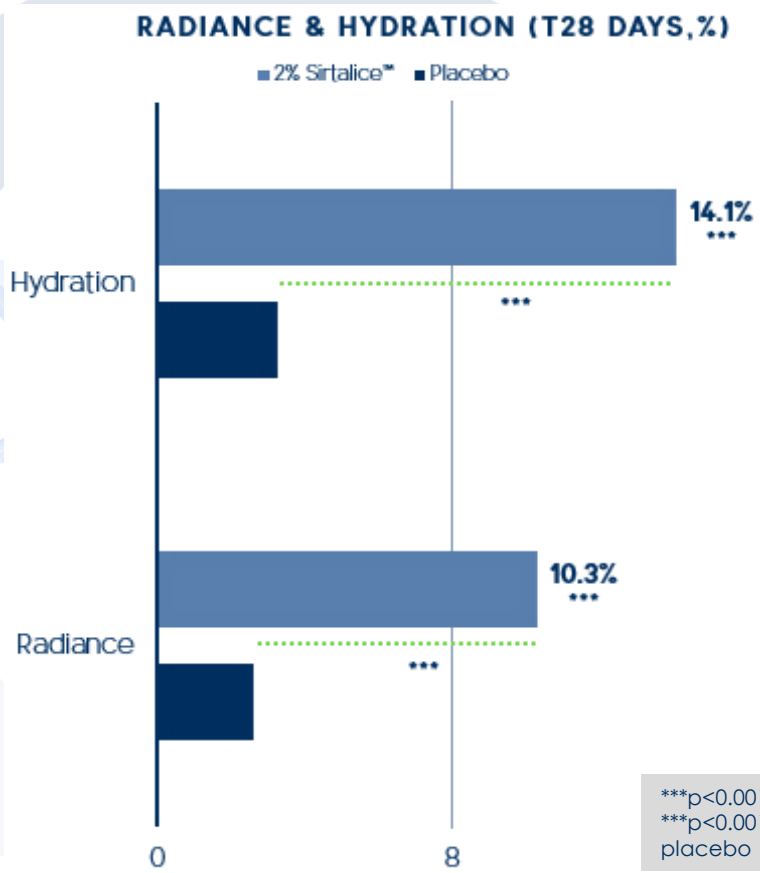
T28 days



Crow's feet depth: ↓37.6%
Crow's feet roughness: ↓18.1%

In vivo efficacy: tightening flash efficacy

- Radiance and hydration (Colorimeter, Corneometer®)
- Cream with 2% Sirtalice™ *vs* placebo
- Half face, 28 days, twice daily
- Age: 35-45



***p<0.001
***p<0.001 vs placebo

✓**10% and 14% more radiant and hydrated skin in 28 days, respectively**

In vivo efficacy: tightening flash efficacy

- Radiance and hydration (Colorimeter, Corneometer®)
- Cream with 2% Sirtalice™ *vs* placebo
- Half face, 28 days, twice daily
- Age: 39 (volunteer 16)

T0 days

T28 days

Radiance: ↑15.1%
Hydration: ↑14.7%

SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

In vivo efficacy: tightening flash efficacy

- Cream with 2% Sirtalice™ *vs* placebo
- Half face, 28 days, twice daily
- Age: 43 (volunteer 10)

T0 days

T28 days

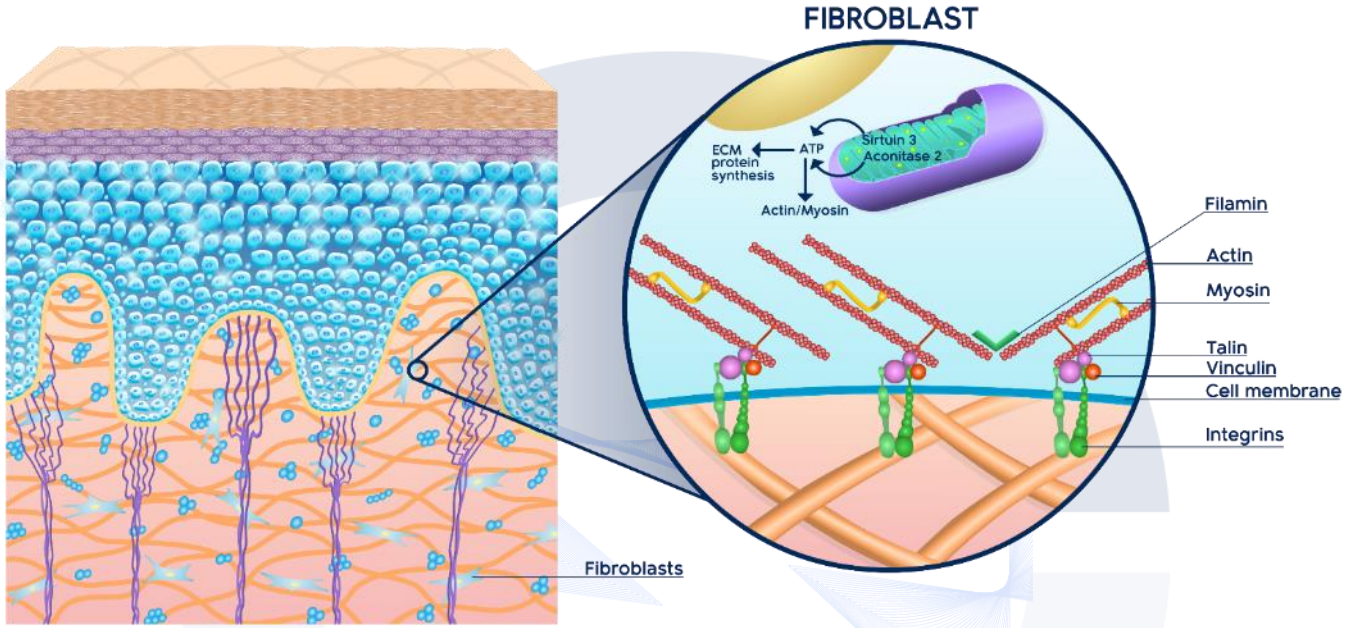
Crow's feet depth: ↓23.9%
Crow's feet roughness: ↓4.5%
Underneath eye wrinkle depth: ↓33.9%
Underneath eye wrinkle roughness: ↓11.6%
Elasticity: ↑12.1%
Firmness: ↑7.8%
Radiance: ↑4.7%
Hydration: ↑13.2%

LIPOTRUE
science & biotechnologies

SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

A freezing blast from the deep sea

- ✓ **Recharges your skin**, boosting cellular energy and **skin contraction**
- ✓ **Reinforces** skin cohesion, enhancing focal adhesions
- ✓ **Instant lifting & V-shape effect** with long-lasting efficacy



SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

Technical information

- **Product Name**: Sirtalice™
- **Marine** active biotechnological ingredient
- **Recommended dose:** 2%
- **INCI name**: Bacillus Ferment
- **Appearance**: Solution
- **Preservatives:** None
- **Solubility**: Water soluble

SIRTALICE™
A FREEZING BLAST FROM THE DEEP SEA

Applications

Cosmetic formulations

- On-the-go good skin day
- Always ready-selfie
- Instant V-shape effect
- Quick fix for busy lifestyles
- Energy blast for your skin
- Deep sea instant refreshing beauty

LIPOTRUE
science & biotechnologies

LIPOTRUE
science & biotechnologies

SIRTALICE™

A FREEZING BLAST FROM THE DEEP SEA

V-lift in
30 min!