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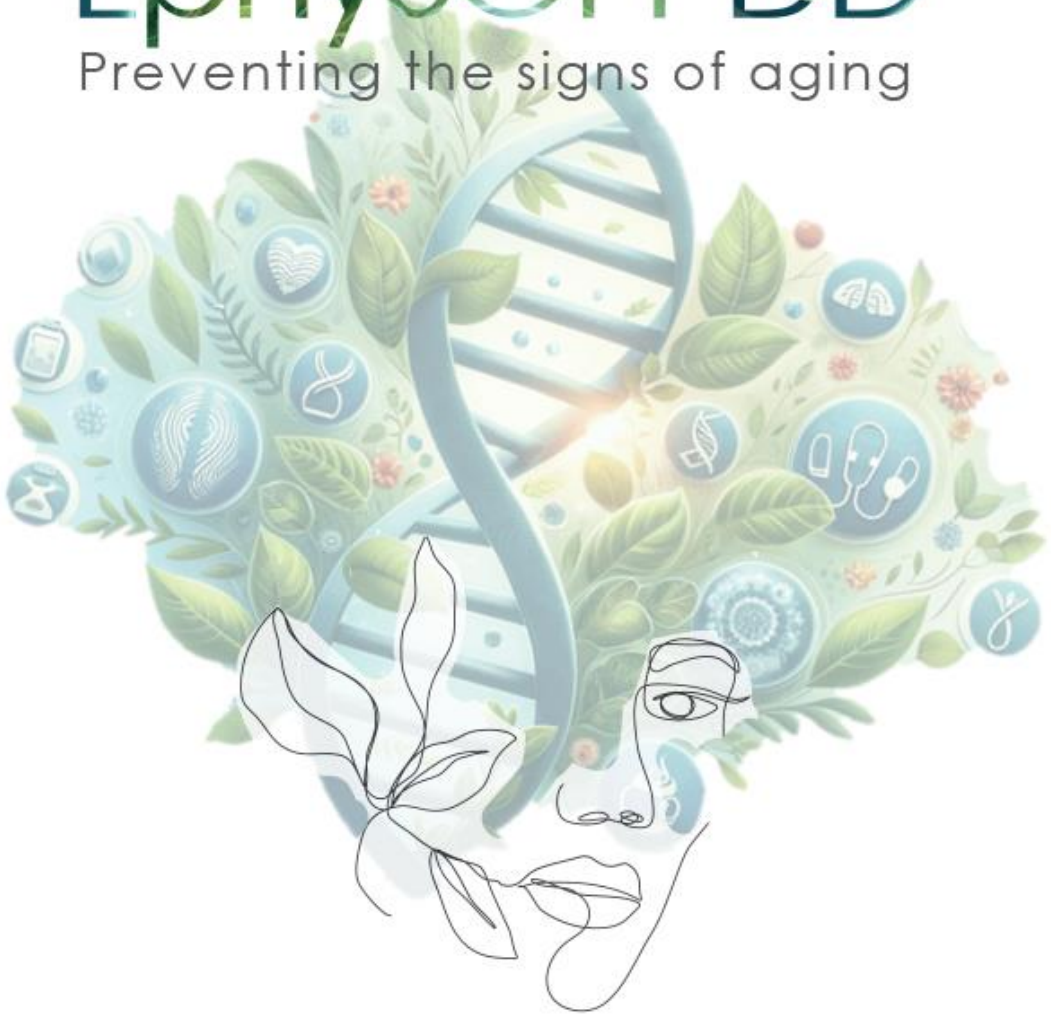
Natural Active Design

EphySOFT DD

Preventing the signs of aging



A road map to everyone true potential: Hallmarks of aging

The evolutionary theory of aging has set the foundations for a comprehensive understanding of aging.

In 2013, López-Otín and colleagues listed and described the "hallmarks of aging," i.e., cellular and molecular interconnected mechanisms involved in human aging[1].

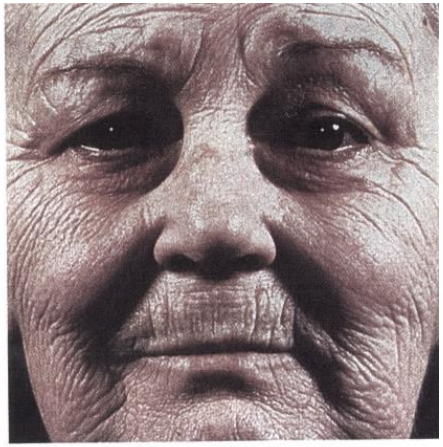
In 2022, during the Copenhagen ageing meeting, a consortium of renowned research institutes completed the list with 6 new hallmarks[2].

Same DNA, Different Epigenetics
TWINS example

Chronological aging

Skin not exposed to UV

Actinic aging



UV-exposed skin

The critical outstanding questions are:

- Can aging processes be slowed down or even restored?
- Can we reverse our epigenetic clock?

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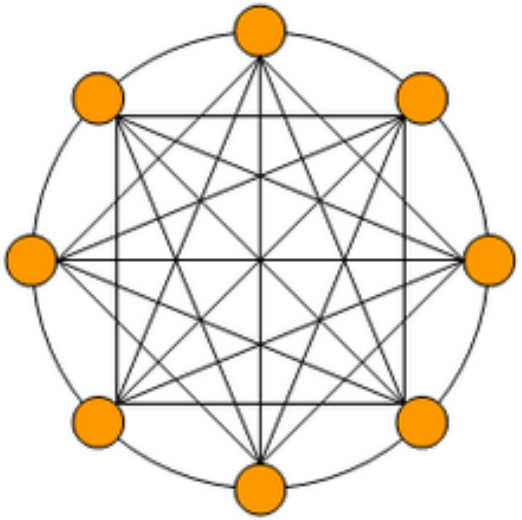
A road map to everyone true potential: Hallmarks of aging

- **Action:** Primary hallmarks of aging (causes of damage)
  - Epigenetic alterations #1
  - Genome instability #2
  - Telomere shortening #3
  - Splicing dysregulation #14
- **Reaction:** Antagonistic hallmarks (responses to damage)
  - Deregulated nutrient sensing #7
  - Mitochondrial dysfunction #10
  - Cellular senescence #5
  - Compromise autophagy #11
  - Inflammation #9
- **Expression:** Integrative hallmarks (impact on the phenotype, visible marks)
  - Stem cell exhaustion #4
  - Loss of proteostasis #6
  - Altered mechanical properties #8
  - Altered intercellular communication #12
  - Microbiome disturbance #13



These hallmarks are interconnected

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Beyond wellness, Wellbeing: Hallmarks of aging

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Preventing the signs of aging

3) Expression: Integrative hallmarks (impact on the phenotype, visible marks)

2) Reaction: Antagonistic hallmarks (responses to damage)

1) Action: Primar hallmarks of aging (causes of damage)

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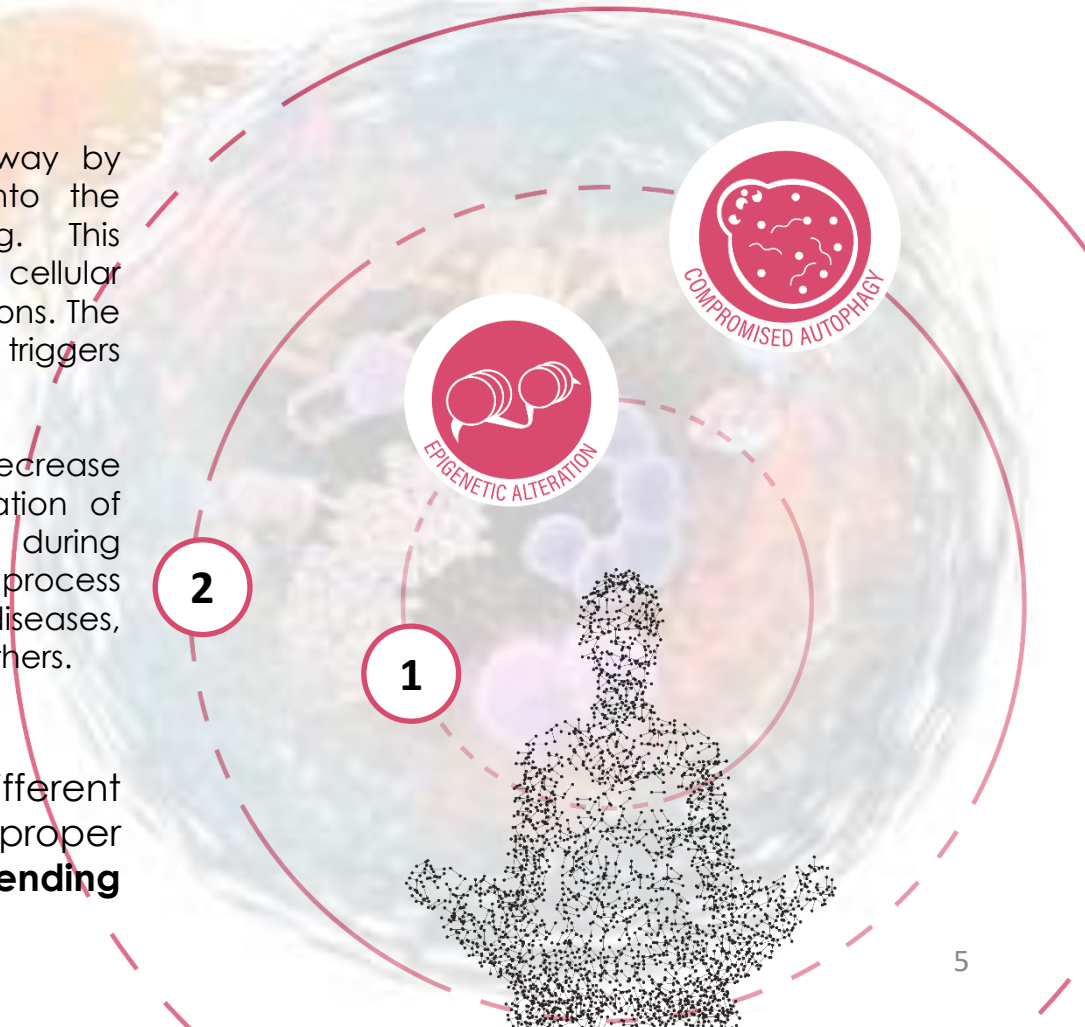
Hallmarks of aging # 1, 11

Autophagy and Aging

Autophagy is a major protein turnover pathway by which cellular components are delivered into the lysosomes for degradation and recycling. This intracellular process is able to maintain cellular homeostasis, and to adapt it under stress conditions. The dysregulation of cellular homeostasis triggers physiological alterations.

The autophagic activity has been found to decrease with age, likely contributing to the accumulation of damaged macromolecules and organelles during aging. Interestingly, failure of the autophagic process has been reported to worsen aging-associated diseases, such as neurodegeneration or cancer, among others.

Good to know : it has been proposed in different organisms that maintenance of a proper **autophagic activity** contributes to **extending longevity**.



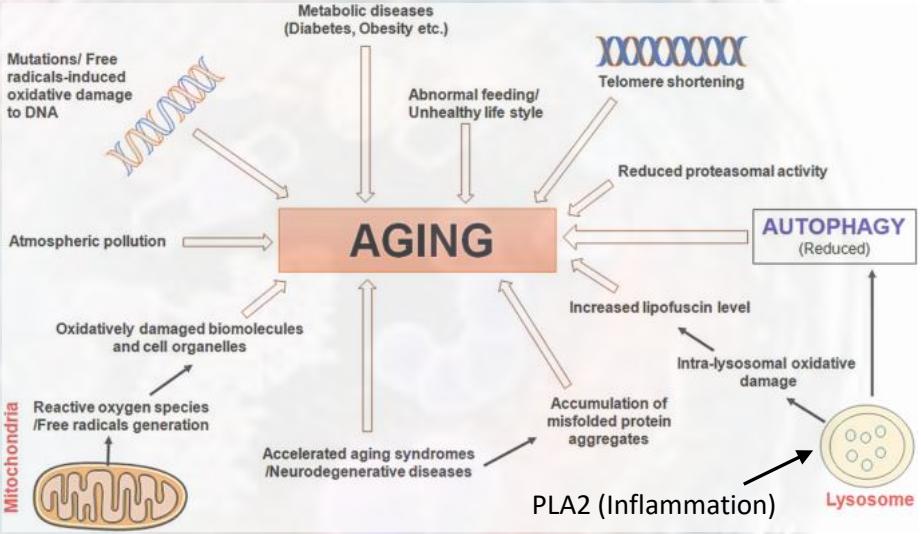
Hallmarks of aging # 11,9,10

Autophagy and Aging via inflammation

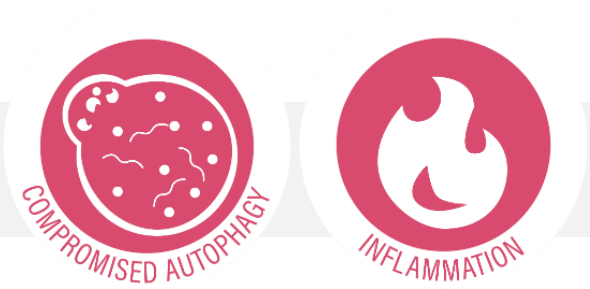
A popular aging theory is the "Stochastic Theory," which suggests that aging results from random damage accumulation. This can be due to external and internal sources over time, in addition to a **failure** of the repairing capacity, such as **autophagy**.

Phospholipase A2 (PLA2) is an enzyme mainly responsible for intracellular phospholipid hydrolysis, which is related to intracellular **inflammation** and participates in the intracellular signaling transduction[3]. **PLA2** can damage cell organelles, and especially **mitochondria** which can lead to promotion of cell death owing to **reduced ATP** and over production of reactive oxygen species (ROS_Free radicals). However, an efficient **autophagy** can remove these damaged mitochondria, thus reducing the pathological response[4, 5].

Good to know : The Inhibition of PLA2 *in vivo* decreases lysosomal damage and restores **autophagy flux.**



Different factors that contribute to the progression of aging- and age-related degenerative diseases[6].



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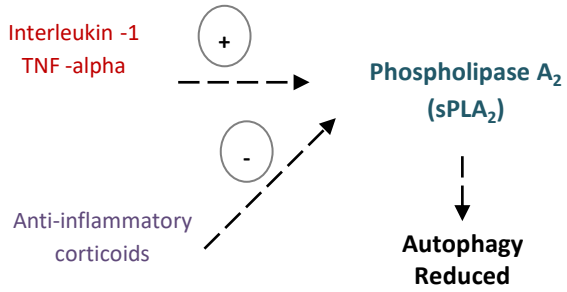
Hallmarks of aging # 11, 9

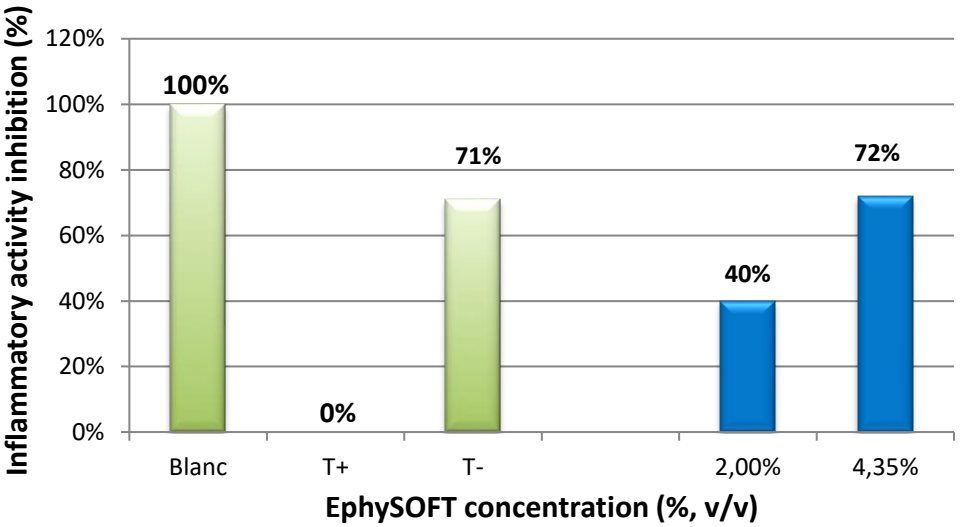
PLA2 Inhibition

A soothing (anti-inflammatory) action can be demonstrated by the inhibition of the enzymes involved in the cascade of arachidonic acid, in particular PLA2.

The Inhibition of PLA2 has the ability to restore **autophagy.**



Evaluation of the inflammatory activity modulation by an acellular *In Vitro* model (PLA2)



Material and method: Enzymatic test *In Tubo* evaluating the inhibition of the basal activity of the PLA2 (V) (basal activity reduced to zero in this graph). Test carried out in triplicate with negative control Thioetheramide-PC 1mg.

EphySOFT DD is a powerful PLA2 inhibitor

EphySOFT DD inhibits PLA2 by **40%** at the 2,0% dose, and provides a further inhibition of **72%** at the 4,3% dose.

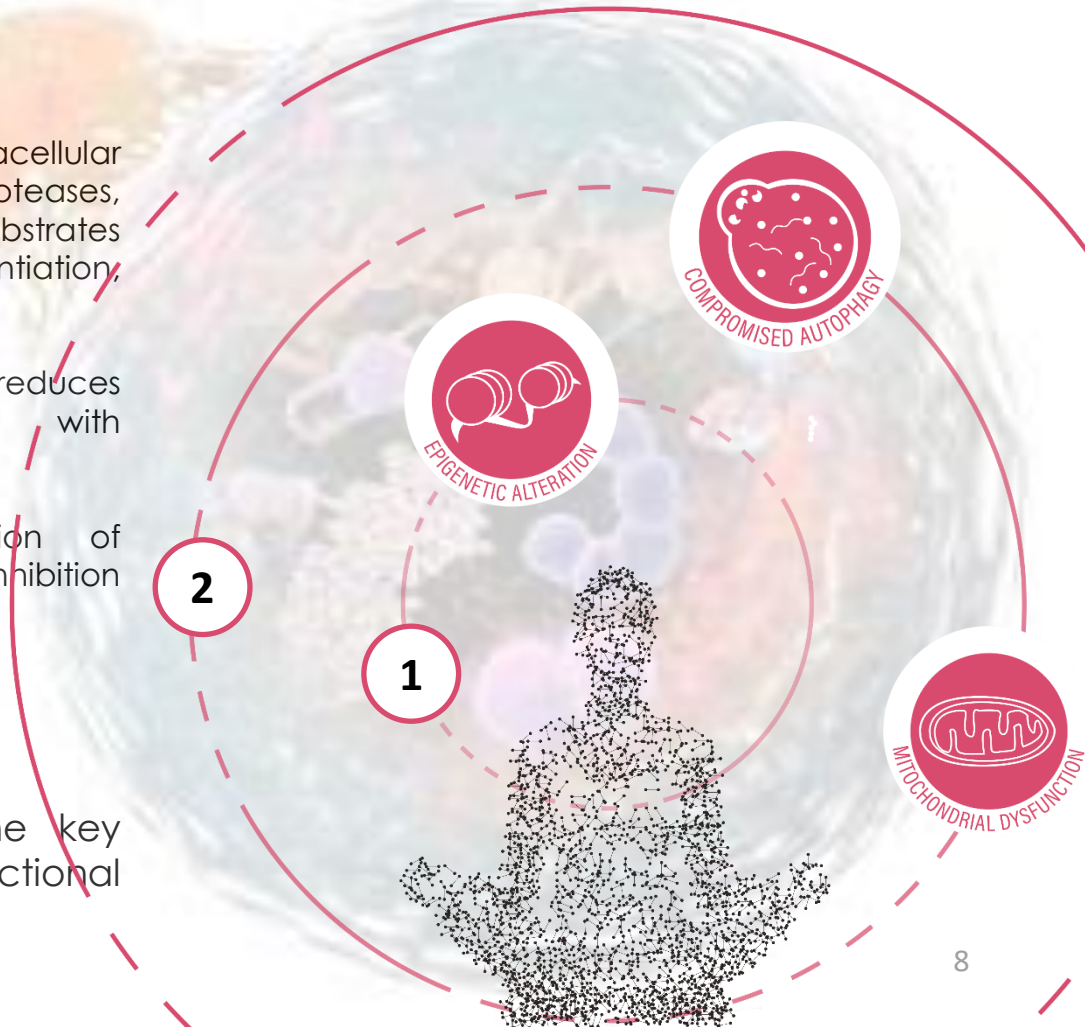
Hallmarks of aging # 1,10,11

Calpain and Autophagy

- Calpains constitute a family of sixteen intracellular nonlysosomal Ca^{2+} regulated cysteine proteases, mediating regulatory cleavages of specific substrates involved in a number of processes during differentiation, life and death of the cell[7].
- Calpain inhibition restores autophagy and reduces mitochondrial fragmentation, concurrent with maintenance of ATP production.
- Restoration of autophagy and prevention of mitochondrial fragmentation via calpain inhibition improves vascular integrity[8].

Good to know :

Calpain inhibitors restore **autophagy**, the key process for maintenance of functional **mitochondria** and **ATP** production[8].

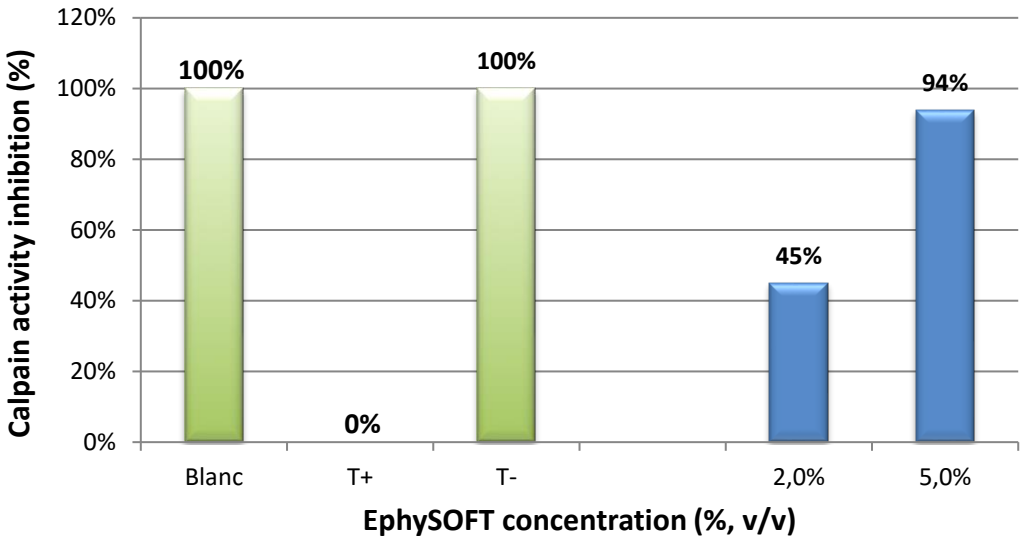


Hallmarks of aging # 1,10,11

Calpain inhibition

At the intracellular level, inhibition of calpain restores autophagy and acts to prevent mitochondrial degradation coupled with an ATP production level maintenance.

Evaluation of the calpain activity modulation by an acellular *In Vitro* model

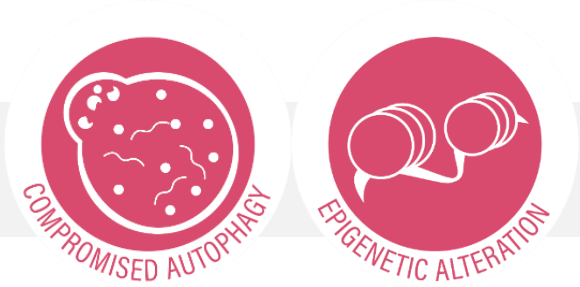


Material and method: Enzymatic test_*In Tubo* evaluating the increase of the basal activity of the enzymes (basal activity reduced to zero in this graph). Test carried out in triplicate with a negative control = Calpain Inhibitor B27-WT.

Ephysoft DD is a calpain inhibitor.

Ephysoft DD has the ability to promote autophagy which preserves the **integrity of mitochondria** and the production of **ATP**.

EphySOFT DD inhibits Calpain activity by **45%** at the 2,0% dose, and provides a further inhibition of **94%** at the 5,0% dose.



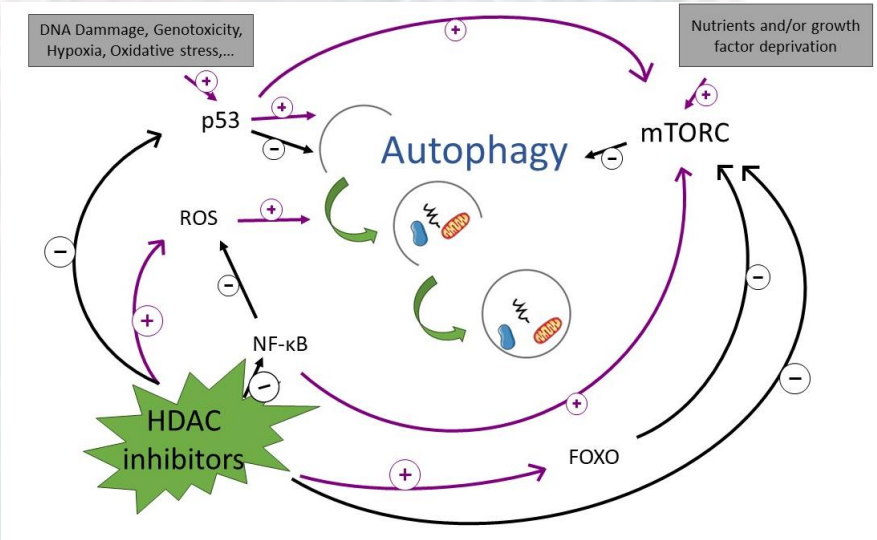
Hallmarks of aging # 1, 11

HDAC inhibitors and Autophagy

Autophagy is a complex pathway modulated (directly or indirectly) by different molecules and mechanisms like transcription factors, tumor suppressors, ROS, Oxidative stress, nutrients and/or growth factors deprivation,…

Among all the best-known modulators, **Histone deacetylase (HDAC) inhibitors are key molecules which can** induce **autophagy**[9,10].

Indeed, inhibition of HDAC (via HDACi) can participate in regulation of various modulators and pathways as inhibition of mTOR, accumulation of ROS or hyperacetylation of NF-κB, resulting in upregulation of p21, or involvement of p53[10,11].



Good to know : HDAC inhibitors are the best positive modulators involved in **autophagy**[9,10].

Hallmarks of aging #1,2,11

HDAC inhibition

This epigenetic action is reversible, it marks a pause in cell, particularly at the level of the cell nucleus. This pause time is used to diagnose the state of the genes with 2 signaling pathways:

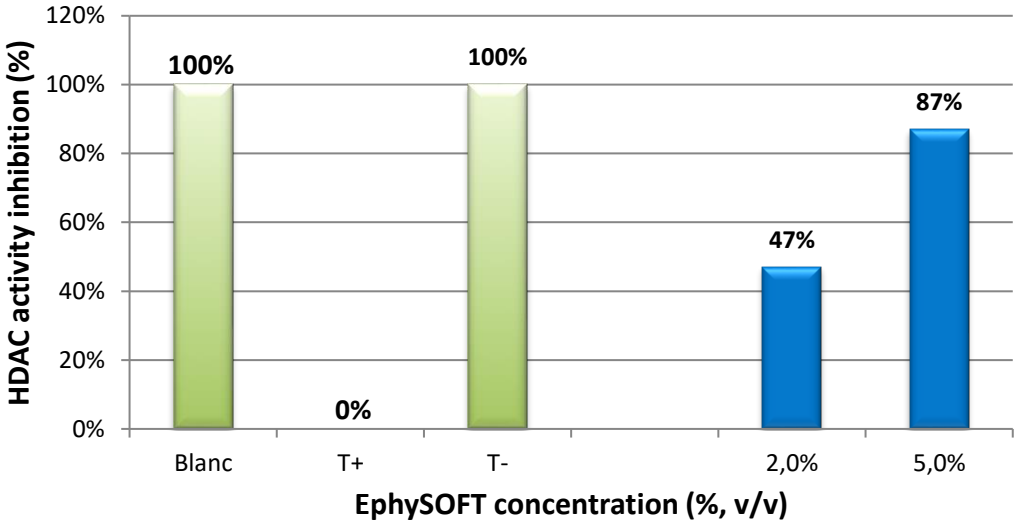
1) if the diagnosis does not perceive a defect or simply minor deviations, then the restoration process is set up using the autophagy process which degrades and recycles the deviant compounds and organelles to be replaced;

2) if the diagnosis detects significant defects or irreparable deviations, then the process of apoptosis takes place and is initiated by autophagy.

EphySOFT DD is a powerful HDAC inhibitor

This particularity makes it possible to erase cellular defects and eliminate unsuitable cells.

Evaluation of the sirtuin I & HDAC enzymatic activity modulation by an acellular *In Vitro* model



Material and method: Enzymatic test_*In Tubo* evaluating the inhibition of the basal activity of the HDAC (basal activity reduced to zero in this graph). Test carried out in triplicate with negative control Trichostatin.

EphySOFT DD inhibits HDAC by **47%** at the 2,0% dose, and provides a further inhibition of **87%** at the 5,0% dose.

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EphySOFT DD Upcycling and sustainability

UpCycling Design

- Our **Desert Date seed oil** activity is located in **West Africa**, Senegal and Burkina Faso where we produce several tons of oil each year to provide the international cosmetic market.
- The main by-product of the first cold pressed oil is the "press cake". This latter contain an unique composition with an intrinsic great biological value.
- This biological potential is unveiled by a specific hydrolyzation process leading to the **Ephysoft DD.**

A Sustainable Supply Chain

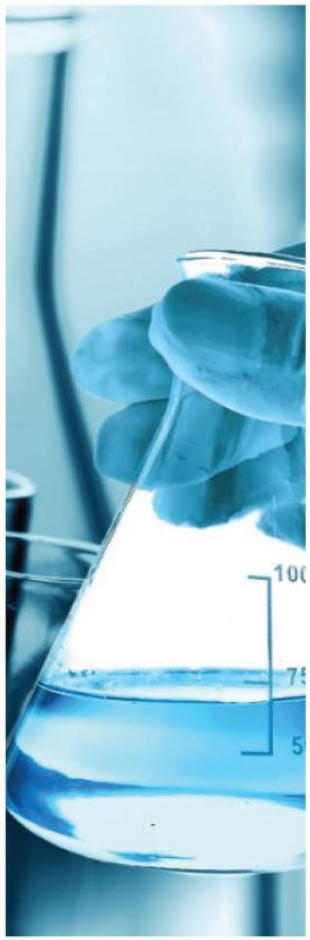
- This « supply chain » involves a plant « ***Balanites aegyptiaca*** ». It is an arid savanna plant found especially on the entire periphery of the Sahara. This plant actively participates in the green belt which aims to fight against the advance of the desert.
- Ephyla **Nursery** Program :15000 shrub plants per nursery (18-month cycle) strengthening of the **green belt.**

EphySOFT DD An integrated approach

Cooperative and ethical approach

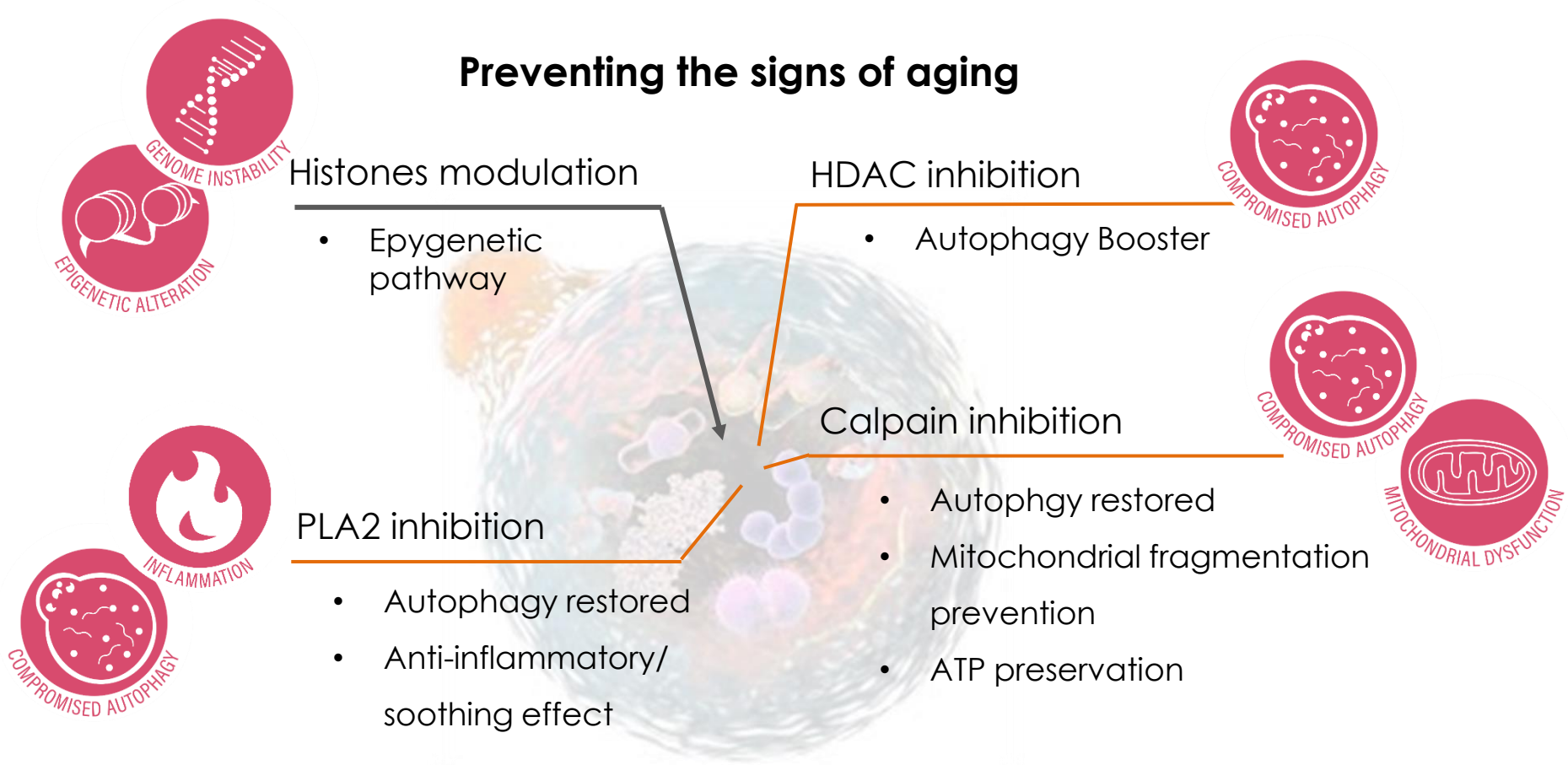
Respect and preservation of the ecosystem

R&D: byproducts valorization



Resources and income sharing

EphySOFT DD, Skin benefits



A road map to everyone true potential

EphySOFT DD, technical data sheet

- INCI: Aqua, Sodium citrate, **Hydrolyzed vegetable protein**
- CAS: 7732-18-5 & 6132-04-3 &100209-45-8
- Einecs: 231-791-2 & 200-675-3 & 309-353-8

- APPEARANCE: beige to yellowish liquid (Room Temperature)

- FORMULATION: Water-soluble

- STORE CONDITIONS: 18 months in a ventilated area

- DOSE OF USE: 2 - 5%

- TOLERANCE:
  - Skin irritation: non-irritating
  - Eye irritation: moderate irritation
  - Phototoxicity: not phototoxic
  - Mutagenicity (AMES): not mutagenic & not pro-mutagenic

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- Be inspired by nature -

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