Addressing skin firmness through DNA methylation

ADEBIOTECH - Romainville | March 13, 2018

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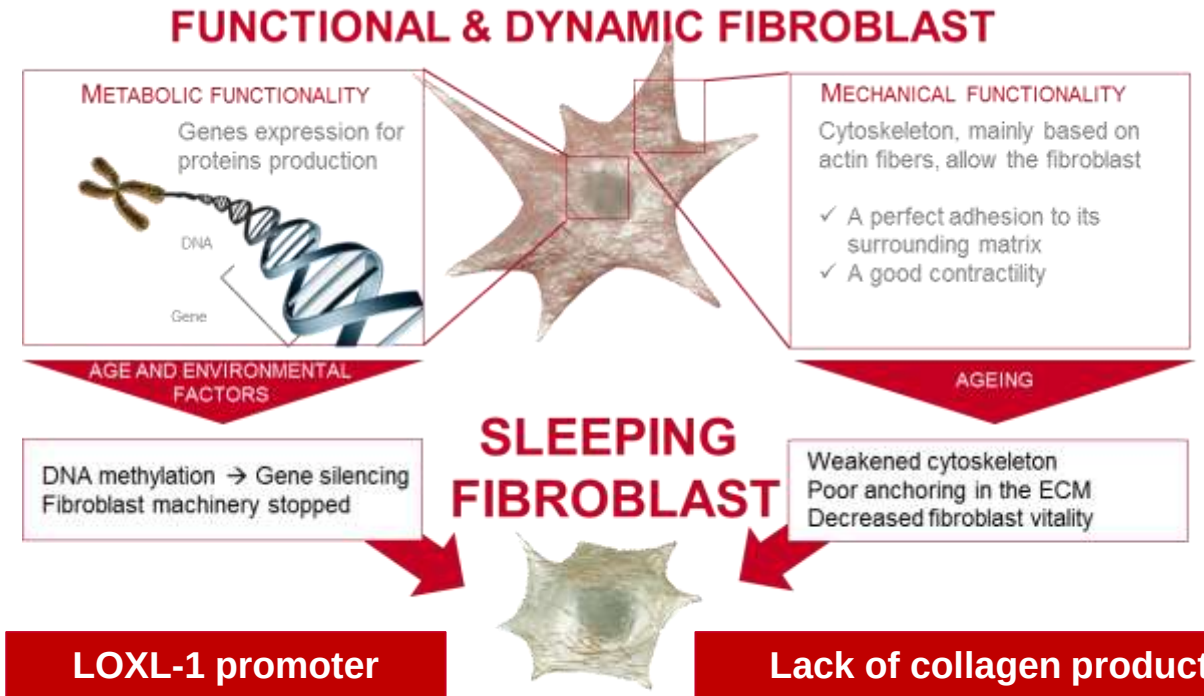
The fibroblast submitted to the proof of time and lifestyle



LOXL-1 promoter methylation

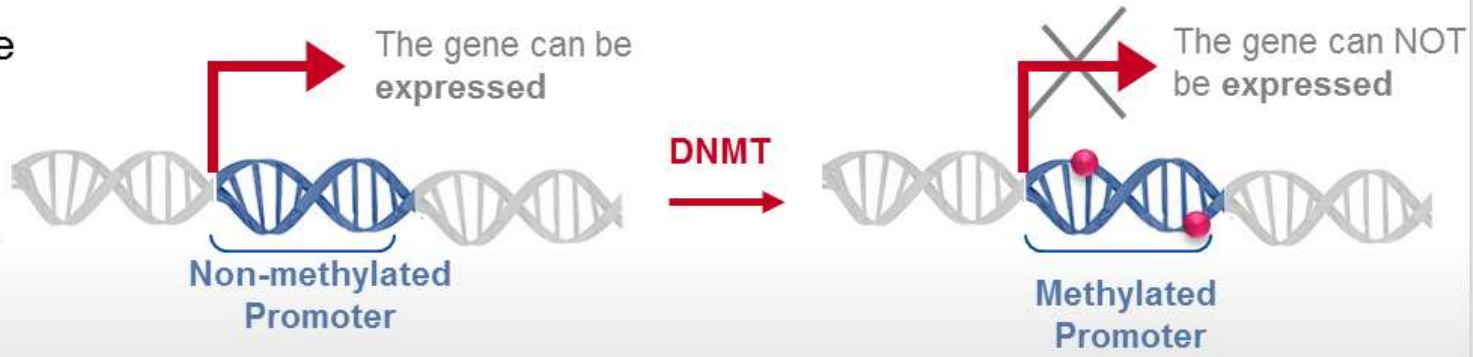
Lack of collagen production
Depleted extracellular matrix

Lack of skin density and firmness

Our Challenge: Wake up our skin cells to reactivate the optimum fibroblast machinery

Epigenetic mechanism through promoter methylation

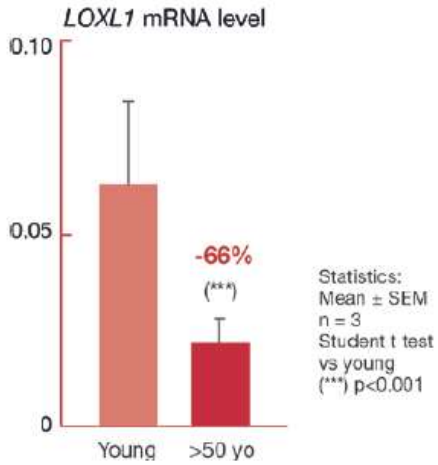
- A **promoter** is a “start signal” region of DNA: indicates where the reading of the gene should start.
- **Methylation of promoter** site **= gene silencing.**
- The methylation reaction needs a catalyzer: the DNMT enzyme.



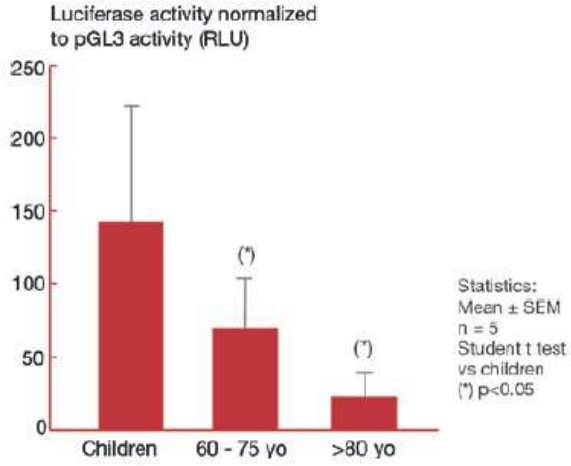
Relationship DNMT3A / *LOXL1* promoter proven in aging

LOXL-1 in elderly fibroblasts

***LOXL1* mRNA expression**

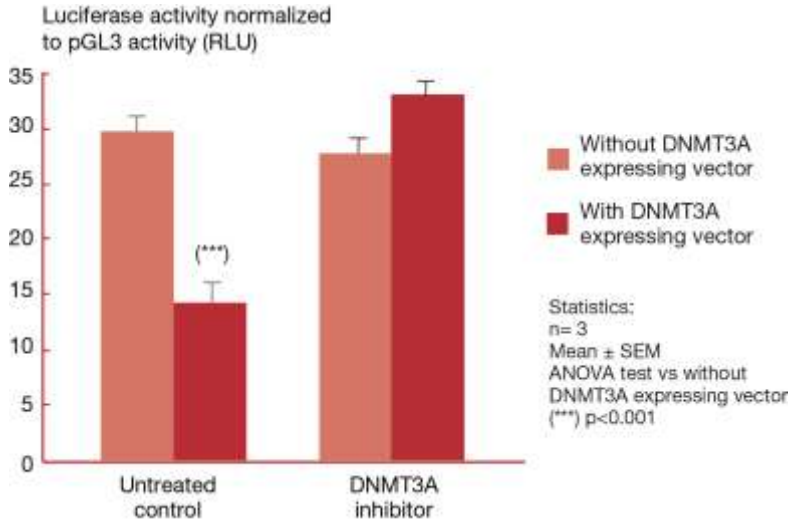


***LOXL1* promoter activity**



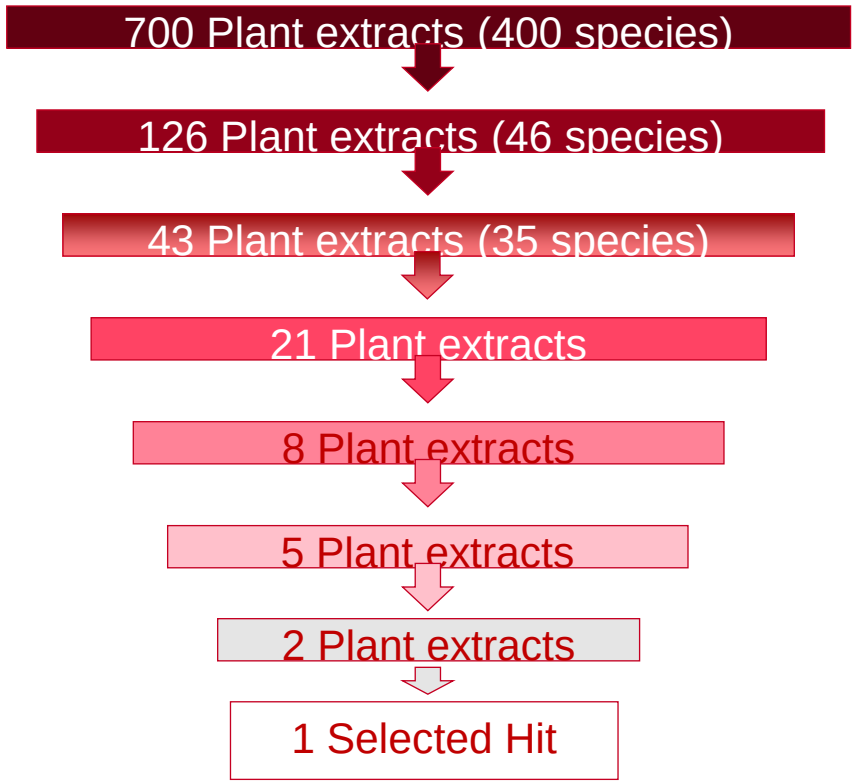
DNMT3A catalytic activity is directly involved in repression of the *LOXL1* promoter activity

Co-transfection of HEK cells with pLL32-luc -/+ pDMT3A



LOXL1 mRNA expression is decreased with aging due to a decrease of its promoter activity which is correlated with an increase of DNMT3A driven methylation

Epigenetic regulation: Screening strategy
To reverse methylation and restore *LOXL1* expression



Preselection in BBCS library

Cell viability and organoleptic assesment of ingredients

Q-PCR screening: Induction of gene expression of 4 genes related to ECM synthesis and organization (*col1a, loxl1, fbln5 and magp1)*

HRM-PCR selection: Decrease *of loxl1* promoter *methylation*

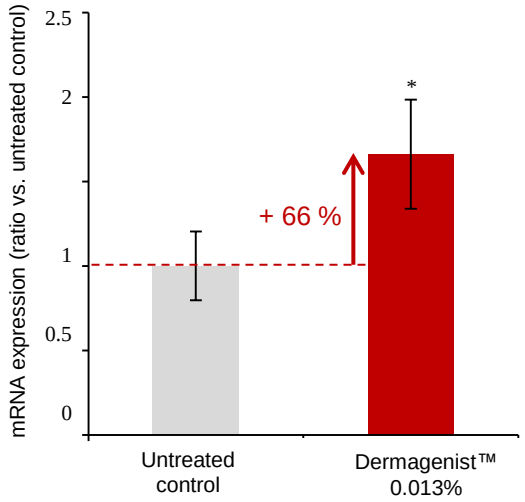
Confirmation: Decrease of recombinant DNMT3A in transitory transfection system

Validation: Induction of Loxl1 and Col1 protein increase in ECM in aged fibroblasts

Origanum majorana extract (Dermagenist™) was selected

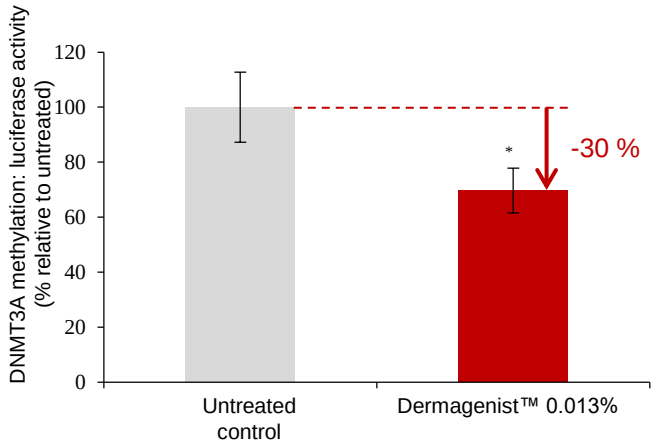
Dermagenist™ reverses methylation and restores *LOXL1* expression

Real-time PCR on aged fibroblasts



Dermagenist™ increases *LOXL1* mRNA expression

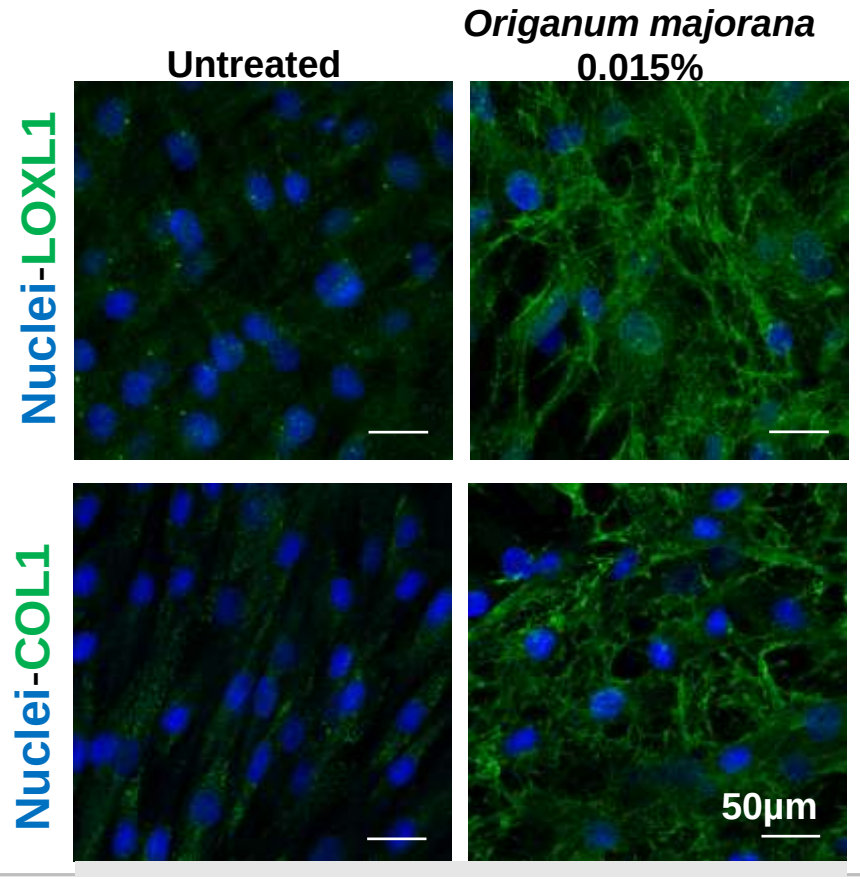
Co-transfection of HEK cells with pLL32-luc -/+ pDNMT3A

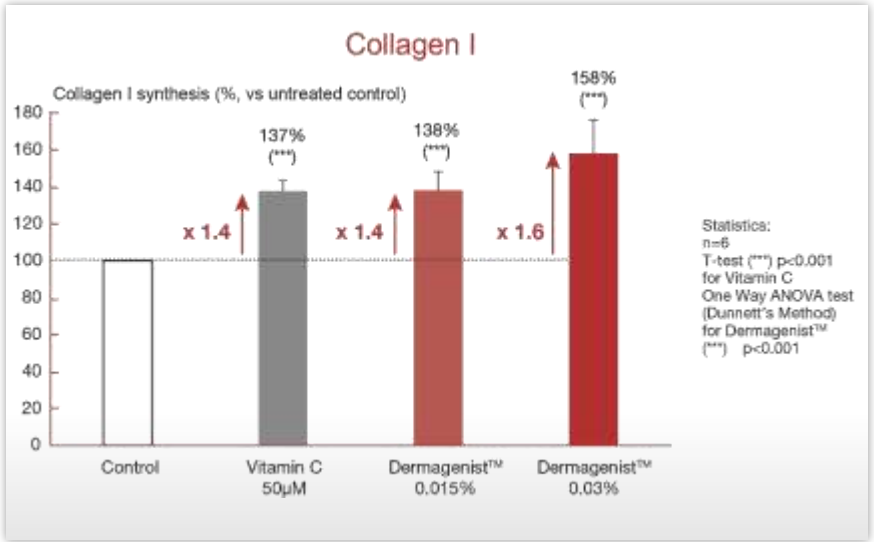


Dermagenist™ reduces DNMT3A-driven methylation

Dermagenist™ prevents the methylation of LOXL1 promoter driven by DNMT3 suggesting a rejuvenation effect of cell's epigenetic pattern

Dermagenist™ induces LOXL1 protein involved in collagen fibers organization





Dermagenist™ reactivates COL I proteins to restore skin firmness

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