# Advanced human 3D-bioprinted skin constructs to model inflamm'aging

Poster 249

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## Introduction:

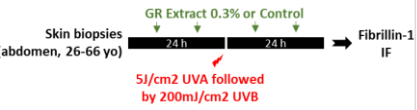
Skin is the largest organ of the human body, directly exposed to the external environment. Throughout its life, human skin is constantly undergoing aggression from different origins, which cumulatively adds to its physiological aging[1,2]. Exposed daily to these various physical or chemical stimuli, an inflammatory-like response can be triggered for the skin to efficiently resist and protect itself. The term inflamm'aging reflects this close relationship between inflammation and aging, concept that originated in the 20's with the "inflammation hypothesis of aging"[3,4].

Micro-inflamed skin displays the classic signs of inflammation that are not immediately visible, the so-called silent or sterile inflammation. Specific mediators of inflammation are produced in small amounts within the skin by cells that are exposed to their environment or in response to their own metabolism. It is the repetition, chronicity, accumulation that eventually alter the physiological balance of the skin leading to a loss of functionality and the appearance of visible aging signs[5]. Importantly, all skin layers are affected by inflamm'aging, as the expression of mediators of inflammation will impact the epidermis structure, its barrier function, and dermal integrity.

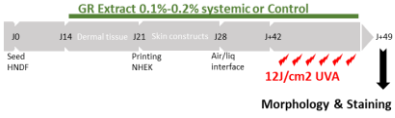
While we gained a lot of insights on the molecular mechanisms driving inflamm'aging using 2D cellular models, a more integrated view is needed to grasp both molecular and cellular consequences on human skin. We used chronic exposure to ultraviolet radiation (UVR), to mimic inflamm'aging on skin models and assess the protective capacity of a new Granville Rose extract (GR extract), prepared with a new advanced eco-extraction method with a process of magnetic waves and centrifugation.

## Materials & Methods:

SKIN EXPLANTS MODEL




3D-BIOPRINTED SKIN MODEL




## Conclusions:

Using skin explants, we could show the deleterious effect of a combination of UVA and UVB on the skin dermal compartment, with disorganized Fibrillin fibers. Treatment with GR extract prevented these deleterious effects.

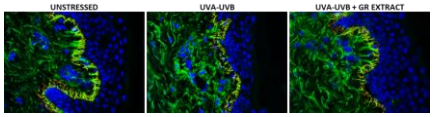
To further mimic inflamm'aging, we used a dose of 12J/cm2 of UVA chronically applied on 3D bioprinted skin constructs. Chronic UVA irradiation strongly affected skin morphology, with a thin, disorganized epidermis, and a defect in epidermal differentiation. The dermal compartment was also impacted, with a decrease in synthesized ECM. Systemic treatment with GR extract rescued all these phenotypes. We furthered demonstrated that GR extract rescued the chronic UVA-dependent loss of filaggrin expression in the epidermis, and loss of collagen III in the dermis. The obtained results were similar to dexamethasone treatment, a pharmacologic drug known for its anti-inflammation properties.

**Altogether, our work describes a new predictive 3D bioprinted model to assess the deleterious consequences of inflamm'aging using UVA chronic inflammation. In addition, we identified GR extract as a key cosmetic ingredient to fight against inflamm'aging on all skin layers.**

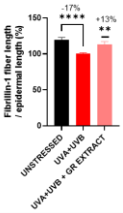
## Results & Discussion:

### GR extract prevents UVA+UVB-induced fibrillin degradation.

SKIN BIOPSIES

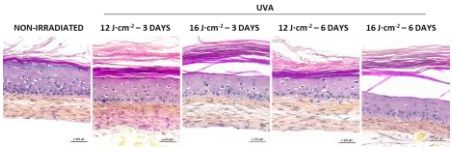


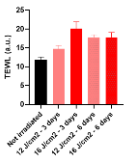

FIBRILLIN / DNA (DAPI) / Fiber network skeleton




=> A combination of UVA and UVB induces fibrillin degradation, improved upon GR extract treatment.

### Chronic inflammation on a 3D bioprinted skin model to mimic inflamm'aging – set-up

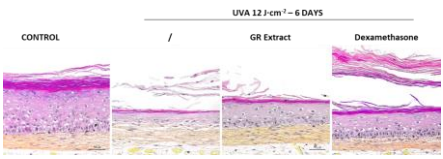


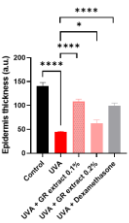




=> Increase of TEWL, disorganized epidermal basal layer, and impaired dermal structure (less dense) following chronic UVA treatment

### GR extract protects 3D-printed skin from chronic UVA-induced epidermis thinning

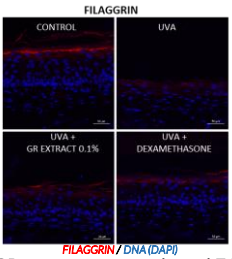
3D-BIOPRINTED SKIN



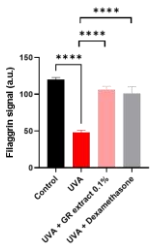




=> Chronic UVA strongly affected skin morphology at the epidermis and dermis levels, rescued by systemic treatment with GR extract

### GR extract protects epidermal differentiation from chronic UVA stress.

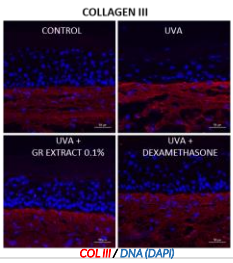



FILAGGRIN / DNA (DAPI)

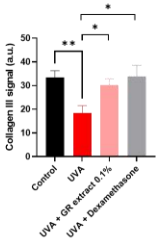



=> Chronic UVA decreased filaggrin expression by 60%, but GR extract restored this expression to a value close to unirradiated controls

### GR extract protects dermal ECM from chronic UVA stress.




COL III / DNA (DAPI)




=> 45% decrease in collagen III expression following chronic UVR. Consistent with the benefits of GR extract observed on the skin morphology, collagen III was protected with the rose extract,

## References:

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[5] P.U. Giacomoni, G. Rein, Textbook of Aging Skin: Skin Aging: A Generalization of the Microinflammatory Hypothesis, in: n.d.