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Epidermis basal cells possess specific mechanical properties, altered during aging

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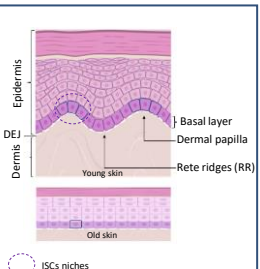
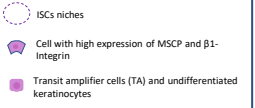
Introduction:

Human skin is composed of the hypodermis, the dermis, and the epidermis. Between dermis and epidermis is found the **dermal-epidermal junction (DEJ)** composed of epidermal rete-ridges (RR) and dermal papilla.



In our study we have focused about the **basal layer** of the epidermis which contains different cells subpopulation including **putative interfollicular stem cells (ISCs)**. Putative ISCs, strongly expressing β1-Integrin and specifically MCSP protein, are organized in **niches** above dermal papilla. Generally, stem cells niches present a **specific environment**. Moreover, the ISCs have **numerous cellular junctions** with **other cells** and with **extra cellular matrix (ECM) proteins**.



Skin aging is characterized by a **flattening of the DEJ**, a decrease in the epidermal renewal, a decrease in the pool of ISCs and a change in the ECM proteins.

In human skin, no consensus has been accepted to confirm the localization of ISCs. Another approach to characterize them is to analyze their **mechanical properties** and in particular their **cell stiffness** by **Atomic Force Microscopy (AFM)**.

Cell stiffness is **influenced** by different factors such as **cell environment**, **cell junctions** and **cytoskeleton architecture**.

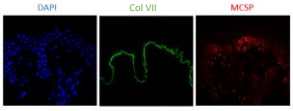
We therefore sought to know if ISCs have specific mechanical properties and if aging impacts them.

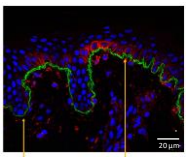
Materials & Methods:

Age-groups and skin sections

Skin explants from plastic abdominoplasties were obtained from donors of 22, 36, 37, 47, 61 and 64yo. 16µm-thick skin cryosections obtained with cryostat (Leica).

Immunofluorescence assay



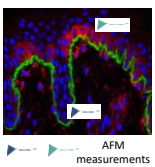


Rete ridges (RR) Dermal papilla

Immunofluorescence assay on 18µm thickness skin sections from woman abdominoplasty (36yo), observed with a confocal microscopy, stained for Col VII (green), MCSP (red), DAPI (blue). Scale bar : 20 µm.

AFM analysis

The AFM system used is a Bioscope Resolve (Bruker, USA) equipped with DMi8 epifluorescence microscope (Leica, Germany).



AFM measurements

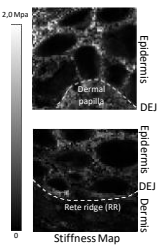
To study the mechanical properties of basal cells of the epidermis we analyzed their cell stiffness. The cellular stiffness of epidermal basal cells was studied from 18 µm thick cryosections of human skin at different ages.

AFM measurements were performed at the level of ISCs above dermal papillae at the level of basal cells above rete ridges on lateral skin cryosections.

Force indentation curves, acquired during the AFM measurements, are used to generate stiffness map from which the average cell stiffness of the basal cells is extracted.

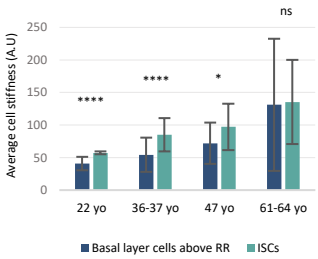
The difference in cell stiffness between the basal layer cell subpopulations was studied by calculating the cell stiffness ratio by using this formula :

$$\text{Cell stiffness ratio} = \frac{\text{Cell stiffness of ISCs}}{\text{Cell stiffness of basal cells above RR}}$$



Results & Conclusions:

ISCs possess specific cellular stiffness



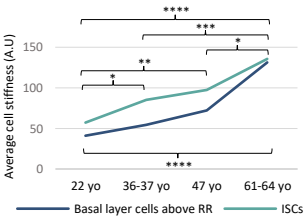
Average cell stiffness of basal layer cells depending on the age of the donor.

ISCs, above dermal papilla, have higher cell stiffness than basal layer cells above rete ridges.

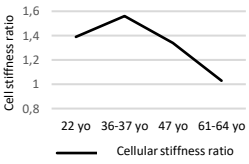
Evolution of th mechanical properties of ISCs during aging

Average cell stiffness of basal layer cells depending on the age of the donor.

Cell stiffness of all basal layer cells increases with aging.



Attenuation of differences in mechanical properties of basal cells during skin aging



Ratio of cell stiffness within basal layer cells between cells supbopulation.

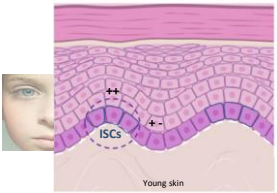
Aging impacts mechanical signature of interfollicular stem cells : ISCs possess a similar cell stiffness as other basal cells located above rete-ridges.

Discussion:

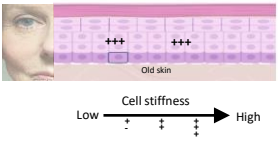
AFM-based approach enables to highlight a specific mechanical properties of interfollicular stem cells.

The interfollicular stem cells have a higher cell stiffness than basal layer cells located above rete ridges.
This higher cell stiffness could result from the numerous cellular junctions between ISCs and other basal cells as well as the proteins of the extra cellular matrix. These junctions can have an influence on the architecture of the cell cytoskeleton.

During aging, the ISCs have the same cell stiffness as the basal cells above the wrinkles.
This can be explained by the modification of the environment of the ISCs during aging : a decrease in the pool of stem cells, a change in the protein composition of the ECM.



Moreover, the topography of the JDE on which the basal cells rest changes during aging due to its flattening.
It has been described that the topography of the substrate on which the cells rests have an influence on cell fate and cell stiffness.



References:

A. Giangreco et al., 2010 ; J. Legg et al., 2003 ; F.M. Watt et al., 2002 ; X. Mu et al., 2020 ; H. Lv et al., 2015 ; S. A. Mobasseri et al., 2019