EVALUATION OF THE IMPACT OF MITOCHONDRIAL FUNCTIONS ON SKIN.

A CELL-TO-SKIN ANTI-AGING STRATEGY

N.ANDRE, C.MONNIN, C.CLAVE, I.THUILLIER, J.GINESTAR

C.F.E.B SISLEY, 3-5 avenue de Friedland, 75008 Paris; nada.andre@sisley.fr

INTRODUCTION

Mitochondria are the power house of cells. Increasing evidence points the fact that an alteration in mitochondrial functions is a potential target of the aging process in skin.

In this paper, we focused on several models that can help evaluating the effect of active ingredients and cosmetic skin care products on the mitochondrial functions of skin cells.

Work was first done on cellular level (*in-vitro*) and then on skin level (explants & RHE). This provides a complete cell-to-skin anti-aging strategy of evaluation.

The following points were studied on the cellular level:

1. Mitochondrial fission and fusion: Mitochondria are highly dynamic cellular organelles, with the ability to undergo the highly coordinated processes of fission (division of a single organelle into two or more independent structures) and of fusion (the opposing reaction). These actions occur simultaneously and continuously in skin cells and the balance between them regulate the overall energy balance and metabolism. Although not fully understood, alteration in the fission/fusion process appears to be involved in several activities that are crucial to the health of skin cells. The MitoTracker probe was used for studying this process (figure 1).

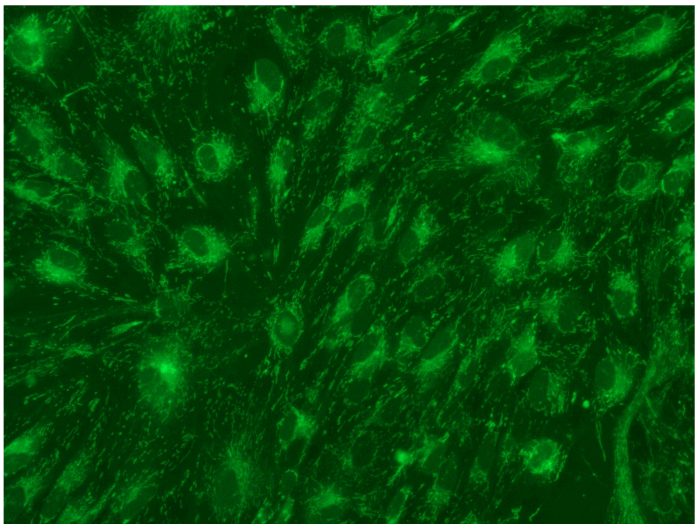

Figure 1 : Fission/Fusion process on skin cells (MitoTracker probe)

2. Wound healing: As an end point of the effect of mitochondrial fission/fusion process, the wound healing capacities of skin cells were studied (scratch wound assay).

The following points were studied on the skin level:

1. Mitofusin 2 (MFN2): MFN2 is a mitochondrial membrane protein that participates in mitochondrial fusion and contributes to the maintenance of the mitochondrial network and regulates mitochondrial metabolism and intracellular signalling. Mourier & al (2015) showed that loss of MFN2 leads to impaired mitochondrial respiration and reduced ATP production. In this study, Mitofusin 2 of skin cells was targeted as a marker of mitochondrial state. MFN2 was studied by immunofluorescence using a specific antibody on skin explants (figure 2)

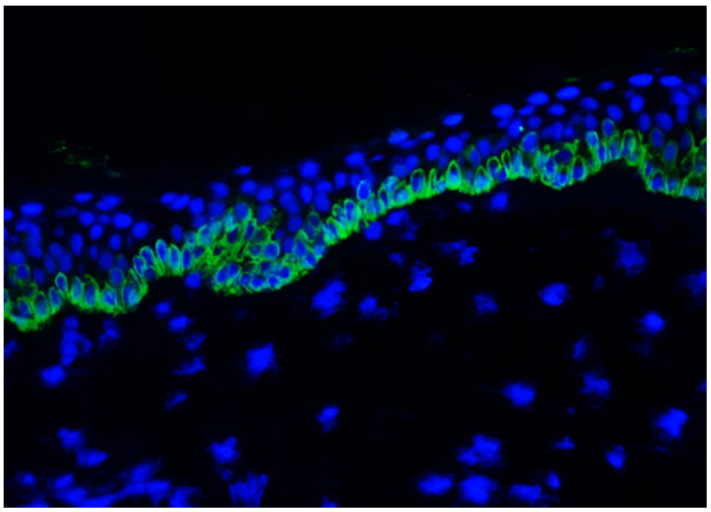

Figure 2 : Sectioned skin explant. MFN2 in green; Nuclei in blue

2. Epidermal thickness: In-house Reconstructed Human Epidermis (RHE) were used to measure the effect of mitochondrial function on the thickness of the epidermis (microscopic observations on cryomicrotomed RHE slices).

SUMMARY OF RESULTS AND CONCLUSIONS

The above described methods seem suitable to evaluate active ingredients and skin care products.

The fission/fusion process was successfully detected and the effect of an oxidative stress (age modeling) was observed.

The effect of an impaired fission/fusion process was highlighted by a decrease in wound healing in skin cells.

On the skin level, the MFN2 protein seems to be affected by an oxidative stress (age modeling). This probably contributes to the accumulation of damaged mitochondria during skin aging leading to impaired mitochondrial respiration and reduced energy production.