EVALUATION OF THE BIOLOGICAL EFFECT OF A HIGH BROAD SPECTRUM SUNSCREEN WITH NICOTINAMIDE AND PANTHENOL REPAIRING PHOTODAMAGED SKIN

G. TELL[(1)], N. CALBET[(1)], J. MATEU[(1)], J. PÉREZ[(2)], B. ALEJO[(2)], P. IGLESIAS[(2)], J. MALVEHY[(1,2)], AL. DEMESSANT-FLAVIGNY[(3)], C. LE FLOC'H[(3)], L. PRIETO[(4)], S. PUIG[(1,2)]

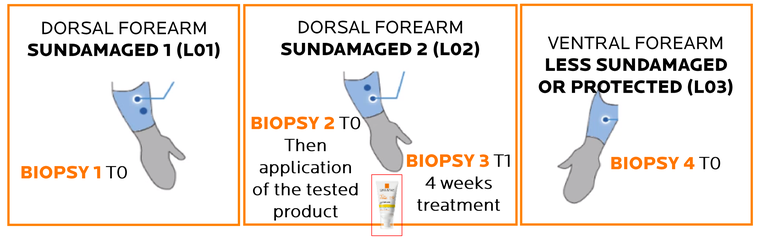
[(1)]Centro de Investigación Biomédica en Red de Enfermedades Raras, CIBERER, Instituto de Salud Carlos III, Barcelona, Spain
[(2)]Dermatology Department, Melanoma Unit, Hospital Clínic de Barcelona, IDIBAPS, Universitat de Barcelona, Barcelona, Spain
[(3)]International Scientific Direction, Laboratoire Dermatologique La Roche-Posay, France
[(4)]Scientific Direction, Laboratoire Dermatologique La Roche-Posay, L'ORÉAL Cosmética Activa, Madrid, Spain

INTRODUCTION & OBJECTIVES

Nicotinamide is a precursor of nicotinamide adenine dinucleotide (NAD), co-enzyme essential in the production of adenosine triphosphate (ATP), main source of cellular energy. Previous studies in mice showed that the oral or topical application of nicotinamide prevents immunosuppression and reduce the number of UV-induced tumors. In humans, topical application of nicotinamide prevents UV induced immunosuppression, but not sunburn. Nicotinamide increases the production of ATP, increases DNA repair and prevents/avoids apoptosis. Only 13 out of 14/15 patients were evaluable with before and after immunochemistry. The main objective of the present study was to determine the biological effect of a high broad spectrum UVB-UVA sunscreen containing Nicotinamide and Panthenol, in photodamaged skin analyzing immunohistochemistry (p53, PCNA, p21 and pyrimidine dimers) and RNA profiles using high throughput technology.

MATERIALS & METHODS

Fourteen healthy patients (> 40 years) were included. Two areas in photodamaged skin in the dorsum of the forearm (area 1 and 2) and one area in the inner part of the forearm less photodamaged (area 3) were identified, imaged optical coherence tomography with lineal confocal OCT and biopsies performed in area 1 and 3. During four weeks, a high broad UVB-UVA sunscreen with nicotinamide and panthenol was applied daily. After that, a new biopsy was performed in area 2 after imaging with lineal confocal OCT. Each biopsy was split into two halves. One was fixed in formalin for ulterior be embedded in paraffin and immunostaining with p21, p53, PCNA and CPD, and the other one was included in RNA*later* and frozen to extract RNA subsequently and carried out the sequencing.

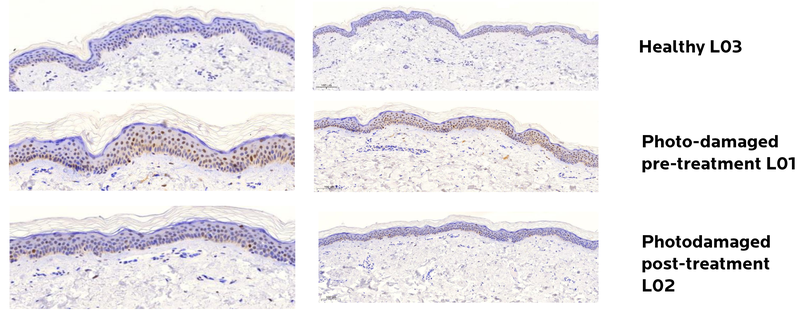


RESULTS

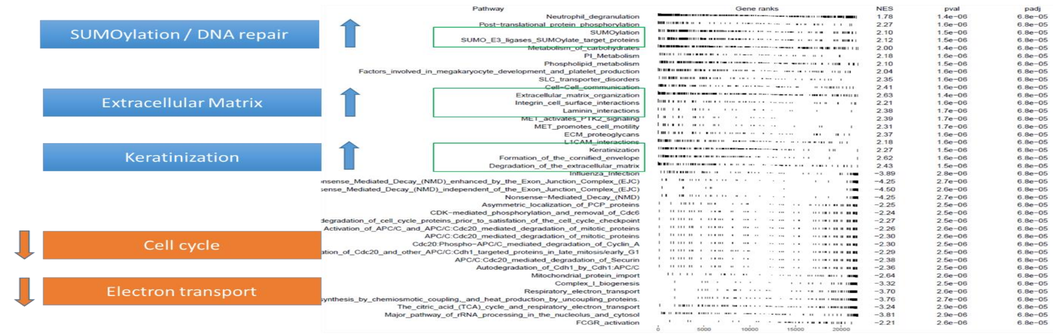
Only 13 out of 14/15 patients were evaluable with before and after immunochemistry comparison (in one patient the post treatment biopsy was not evaluable because of the absence of epidermis in the sample). 100% of cases showed an increased expression of p21, PCNA, p53 and CPD in photodamaged skin (L01) when compared with less damaged skin (L03). After 4 weeks of product application, we identified a slightly decrease of p21 expression in treated photodamaged skin compared to non-treated photodamaged skin (L02 vs L01), but this tendency did not reach statistical significance. Direct comparison pre-post treatment showed significant improvement of p21 expression in 6 cases (1, 6, 7, 8, 13, 14).

Differential gene expression analysis (DGEA) from the RNA-Seq data showed an overexpression of Collagen Type I Alpha 1 Chain *(COL1A1)* gene (adjusted p-value < 0.001) in treated photodamaged skin in comparison with non-treated photodamaged skin (L02 vs L01 biopsies).

Furthermore, the gene set enrichment analyses (GSEA), which took into account the fold-change value for each gene in order to rank them, identified 40 biological pathways significantly dysregulated after treatment (adjusted p-value <0.001). Among the 20 upregulated pathways, there are some related with the SUMOylation process, extracellular matrix organization, cell adhesion molecule activity and keratinization. Otherwise, among the 20 downregulated pathways, several are involved in the reactive oxygen species generation and mitochondrial function.



L02 post-treatment vs L01 Pre-treatment		1 gen overexpressed in post treatment skin		
Ensembl ID	**Gene**	**logFC**	**PValue**	**Adj.P.Val**
ENSG00000108821.14	**COL1A1**	**2.53**	**7.09E-09**	**<0.001**



CONCLUSIONS

Four weeks of daily application of high broad spectrum UVB-UVA sunscreen with nicotinamide and panthenol in photodamaged skin induces overexpression of COL1A1 and influences the regulation of 40 biological pathways involved in the skin homeostasis.

REFERENCES

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