PHOTOPROTECTION FROM UV LIGHT-INDUCED TELOMERE SHORTENING BY A BROAD-SPECTRUM SUNSCREEN PRODUCT

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INTRODUCTION

Chronic UV exposure triggers DNA damage, photoaging, and even carcinogenesis, through the formation of photoproducts and reactive oxygen species, activating DNA damage response (DDR) pathways and ultimately apoptosis or senescence. Telomeres are regions especially sensitive to UV light; their length shortens upon UV irradiation *in-vitro* and *in-vivo*, compromising the regenerative capacity and function of tissues. We aimed to study whether a broad-spectrum sunscreen is able to prevent UV-induced DNA damage and telomeric shortening.

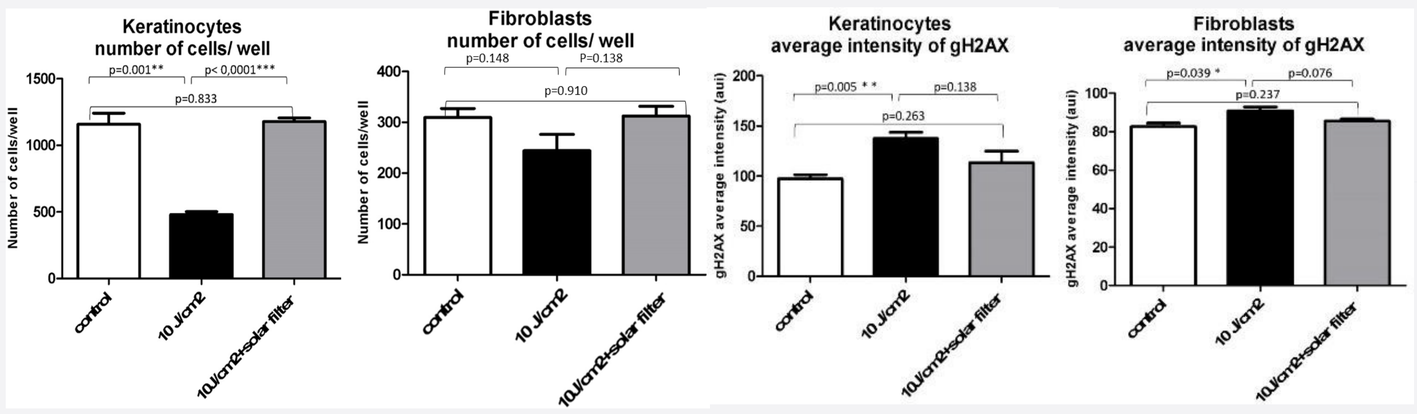
MATERIAL & METHODS

We used in-vitro cultured human keratinocytes and fibroblasts and 3D skin model (EPISKIN™). Three conditions - control, irradiated, and irradiated in the presence of a broad-spectrum sunscreen product, with a very high UVB and UVA protection (SPF 50+ / PF UVA 46)- were compared at 24h post exposure to 10J/cm^2 SSUV using a solar simulator lamp. We used HT Q-FISH as described (Canela *et al.*, PNAs 2007) or FISH on skin slides to measure telomere length, γH2AX immunostaining as a readout for DNA damage, DAPI staining for cell viability, and hematoxylin & eosin staining of skin sections to examine the integrity of the skin structure.

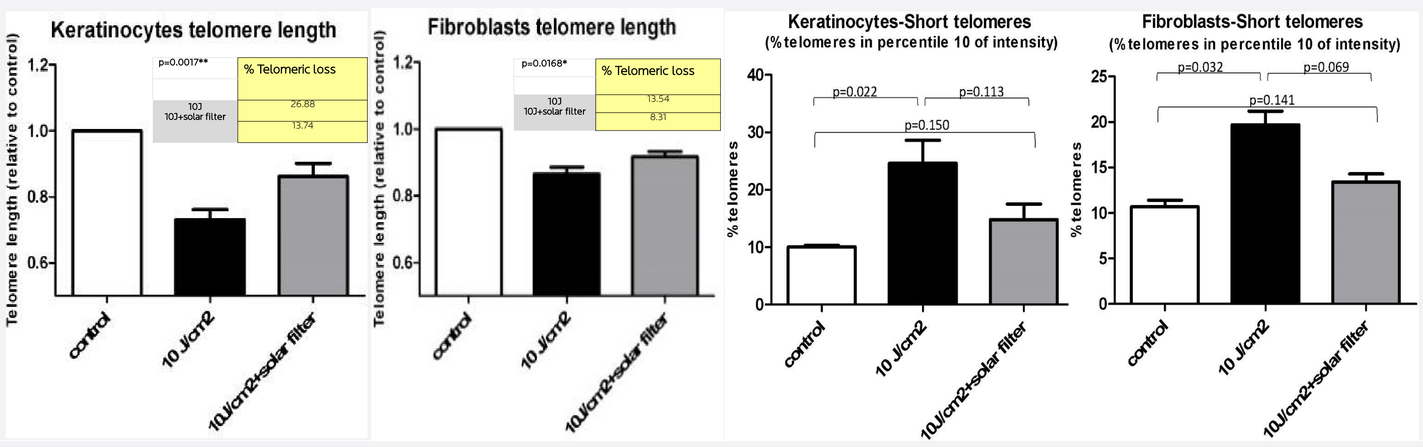
RESULTS

In-vitro cultured keratinocytes and fibroblasts

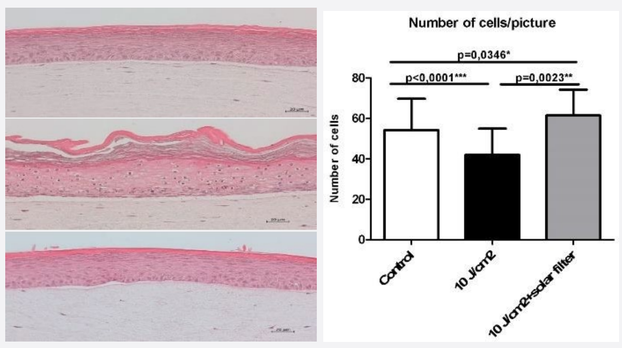
Upon SSUV exposure, there is a reduction in cell viability compared to control (58.4% reduction in keratinocytes and 20.9% in fibroblasts) and increased γH2AX staining. Significantly, in the presence of the sunscreen product, cell viability and γH2AX are comparable to controls.



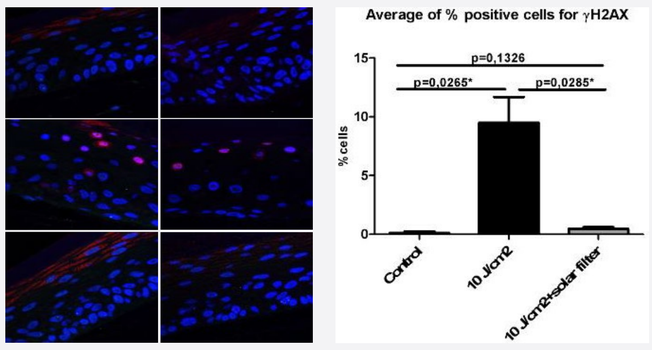
Telomeres are shortened upon UV-light (26.8% and 13.5% of telomeric length loss in keratinocytes and fibroblasts respectively), while in the presence of sunscreen the telomere length is partially preserved (13.7% and 8.3% of telomeric length loss respectively) and the % of short telomeres is reduced.



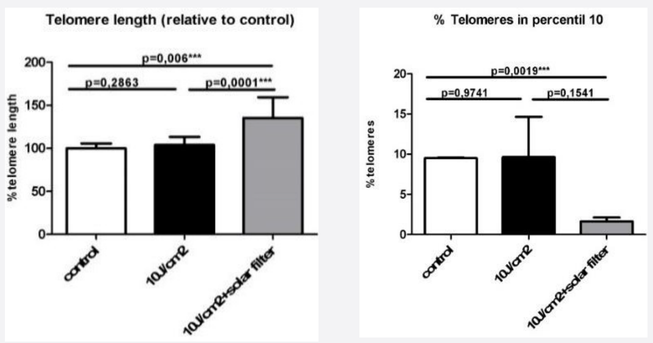
T-SKIN model (EPISKIN ™)



SSUV exposure alters the skin structure and cellularity is reduced to 77.4%. Exposure to SSUV in the presence of sunscreen shows H&E staining and cellularity comparable to controls.



There is a dramatic increase in γH2AX positive cells in UV exposed skin that is completely prevented in the presence of sunscreen.



Telomeres of cells in the 3D skin environment show similar telomeric length upon SSUV exposure to control and this length is even increased when exposure occurs in the presence of the broad-spectrum sunscreen product, together with a decrease in the % of short telomeres

CONCLUSION

In UV-exposed *in-vitro* cells or 3D skin model, a broad-spectrum sunscreen product with a very high UVB and UVA protection (SPF 50+ / PF UVA 46) preserves cell viability and reduces DNA damage. In exposed 3D skin, the sunscreen product protects the integrity of the stratified structure of the skin. Importantly, this photoprotection also occurs at the telomere level since UV-induced telomere shortening is greatly reduced in the presence of the sunscreen in *in-vitro* cultures. Furthermore, telomere length is even increased in 3D skin SSUV exposed in the presence of sunscreen. These results help in the understanding of the mechanisms of photoprotection by a sunscreen product against UV-induced damage and are relevant in the fields of skin biology and carcinogenesis

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References:

Rochette PJ, Brash DE. Human telomeres are hypersensitive to UV-induced DNA Damage and refractory to repair. PLoS Genet. 2010 Apr 29;6(4):e1000926.