Sunscreens: Is It Possible to Better Protect Individuals Prone to Developing Skin Cancer?

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Background

- Skin cancer is the most common type of cancer worldwide and disproportionally affects individuals with fair skin complexion
- One of the major determinants of skin cancer is the exposure to solar ultraviolet radiation (UVR)
- It is known that UVR causes elevation of reactive oxygen species (ROS) levels in the skin
- NADPH oxidase 1 (NOX1) is activated by UVR and participates in the generation of ROS
- High levels of ROS cause cellular stress and DNA damage including Cyclobutane Pyrimidine Dimers (CPDs) and 8-oxodG

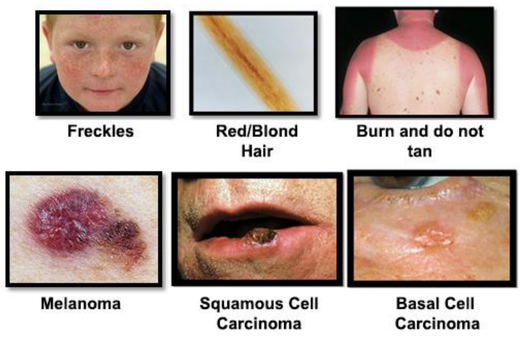

Fig. 1. Individuals with fair skin complexion are more susceptible to developing melanoma and non-melanoma skin

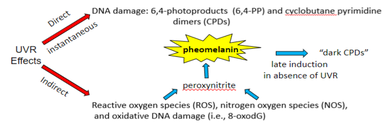

Fig. 2. Direct and indirect pathways for the generation of CPDs induced by UVR

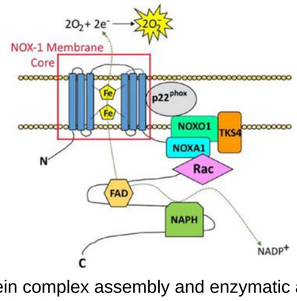

Fig. 3. NOX1 protein complex assembly and enzymatic activation leads to the generation of ROS levels

Objective

Test two inhibitors of NOX1 (NOX-AP2 and NOX_Inhibitor_1) in human skin cells to determine if they can protect against DNA damage

Hypothesis

Inhibition of NOX1 decreases UV induced DNA damage, therefore preventing individuals from developing skin cancer

Results

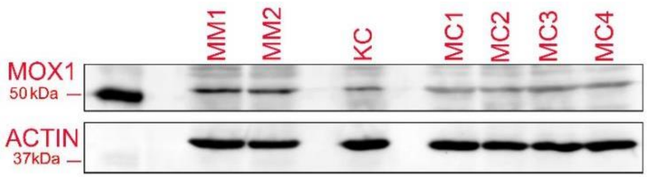

Fig. 4. Expression of NOX1 in normal skin cells (keratinocytes and melanocytes) isolated from human skin

Inhibitor (NOX-AP2)

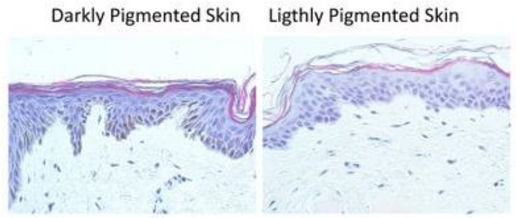

Fig. 5. Histological sections of darkly pigmented and lightly pigmented skin

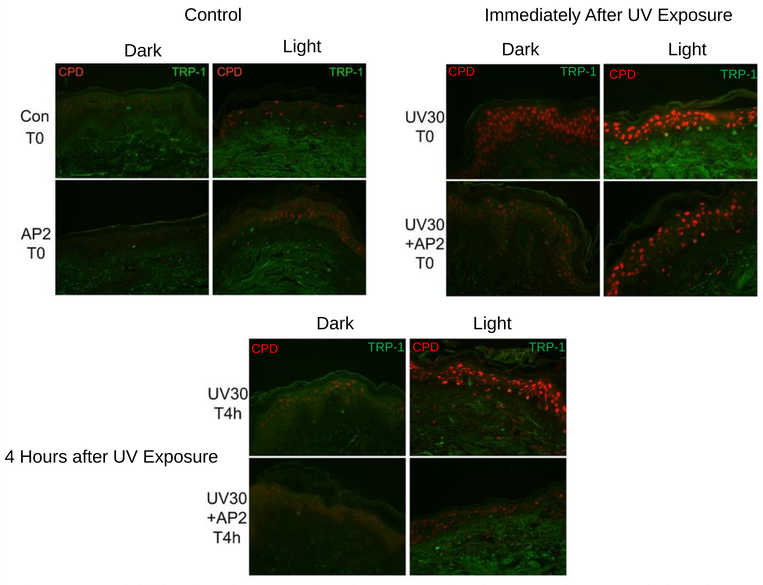

Fig. 6. NOX1 inhibitor (AP2) protects keratinocytes and melanocytes from UVR-induced DNA damage, as shown by the time course of CPD assessment in dark and light skin (T0, T30 min and T4h) after UVR exposure

Inhibitor (NOX_Inhibitor_1)

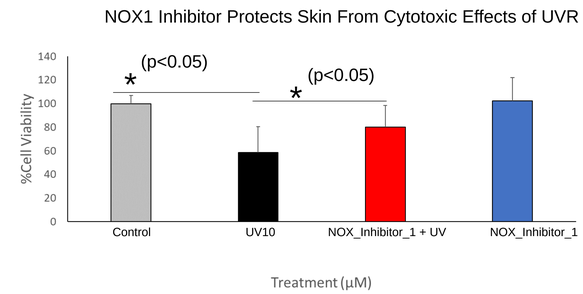

Fig. 7. NOX Inhibitor 1 is not toxic to keratinocytes and significantly counteracts the reduction in cell viability induced by UVR

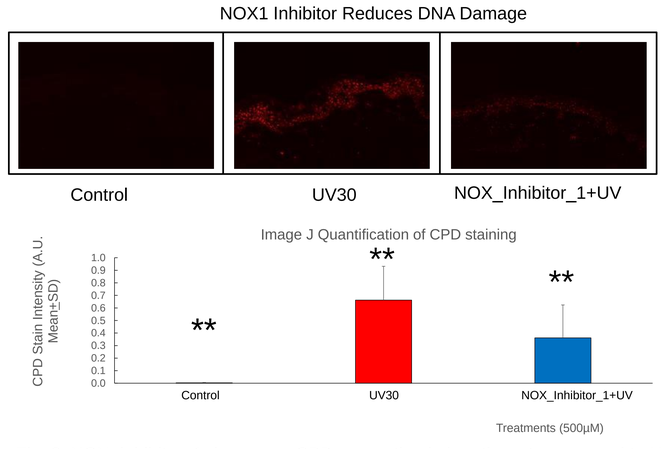

Fig. 8. NOX_Inhibitor_1 decreases CPD generation in keratinocytes exposed to UVR compared to the untreated group

Conclusions

- The two NOX inhibitors tested showed to be non-cytotoxic to skin cells and to protect them from cell death induced by UVR
- Both inhibitors significantly reduced the generation of CPD DNA damage in light and dark skin suggesting that their incorporation into sunscreens could provide enhanced protection against skin cancer

References

1. Panday, A., Sahoo, M. K., Osorio, D., & Batra, S. (2014). NADPH oxidases: An overview from structure to innate immunity-associated pathologies. *Cellular & Molecular Immunology*, *12*(1), 5–23. https://doi.org/10.1038/cmi.2014.89
2. Hirobe, T. (2014). Keratinocytes regulate the function of melanocytes. *Dermatologica Sinica*, *32*(4), 200–204. https://doi.org/10.1016/j.dsi.2014.05.002
3. Mouret, S., Philippe, C., Gracia-Chantegrel, J., Banyasz, A., Karpati, S., Markovitsi, D., & Douki, T. (2010). UVA-induced cyclobutane pyrimidine dimers in DNA: A direct photochemical mechanism? *Organic & Biomolecular Chemistry*, *8*(7), 1706–1711. https://doi.org/10.1039/b924712b

Acknowledgments

I would like to thank Dr. Kadekaro and Alyssa Sterling for mentoring and supporting me through this project