COMBINED EXPOSURE TO UVA1 AND POLYCYCLIC AROMATIC HYDROCARBONS IMPAIRS REDOX HOMEOSTASIS IN HUMAN KERATINOCYTES

Dimitrov A, Soeur J, Belaïdi JP, Denat L, Jones C, Perez P, Zanini M, Zobiri O, Mezzache S, Erdmann D, Eilstein J, and Marrot L.
L'Oréal Advanced Research, Aulnay-sous-Bois, France.
Email: adimitrov@rd.loreal.com

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The skin is exposed to several environmental stresses that differ in nature and intensity. Pollution originating from combustion or industrial processes involves a large range of chemicals. Polycyclic Aromatic Hydrocarbons (PAH) are pollutants present in air, water or food [1]. Due to their ubiquitous presence and toxicity, PAH are important environmental pollutants. Several studies showed that PAH are present in the blood of smokers and individuals living in polluted areas and can be detected in the nanomolar range [2]. PAH are likely to target the skin through topical penetration of ultrafine particles or through systemic distribution. The well-known photo reactivity of some PAH upon UVA exposure could enhance their deleterious effects on skin [3].

Our goal was to investigate in vitro the effects of a combination of PAH and UVA1 on skin cells. This analysis is important since UVA1 represents around 80% of daily UV and penetrates deep into the skin, reaching the dermis.

Here we compared, in *in vitro* cultured keratinocytes, the biological effects of a combined exposure with particulate matter, PM extract or PAH with either daily UV (d-UV 300-400 nm) or UVA1 (350-400nm). Surprisingly, UVA1 alone was associated with an equal or greater phototoxic effect than d-UV.

We then focused on the combined effect of UVA1 with PAH. We show, by spinning disk microscopy, that PAHs are localized in the plasma membrane and in several intracellular compartments in keratinocytes. PAH combined with UVA1 were phototoxic at very low concentrations (15nM per liter), impaired keratinocyte clonogenic potential at subtoxic doses. In a multiple exposure protocol on *in vitro* reconstructed epidermis (RHE SkinEthic, Episkin) this treatment leads to morphological damages in the supra-basal cell layer that we will measure using immunofluorescence and image analysis. 13h post-treatment glutathione neo-synthesis genes (S*LC7A11* or *GCLc)* expression was upregulated and intracellular glutathione concentrations decreased.

In such experimental conditions mimicking skin contamination in a polluted environment, our results suggest that chronic exposure to photo-polluting stress may impair cutaneous homeostasis.

References

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