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Modulation of genotoxic effects of polycyclic aromatic hydrocarbons in human skin upon co-exposure with sunlight

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Co-exposure of skin to carcinogenic polycyclic aromatic hydrocarbons (PAH) and solar UV radiation is of particular interest in occupational safety. Published *in vitro* studies on cultured cells have suggested that UVB enhances the genotoxicity of benzo[a]pyrene (B[a]P) by activating the AhR pathway and overexpressing the cytochrome P450 enzymes responsible for the conversion of B[a]P into DNA damaging metabolites. Our present work involves more realistic conditions, namely *ex-vivo* treatment of human skin explants and simulated sunlight (SSL) as a UV source. We first found that SSL, applied either before or after topical application of B[a]P, led to a lower expression of cytochrome P450 genes than with B[a]P only. Accordingly, the level of DNA adducts to the diol epoxide metabolite of B[a]P (BPDE) was lower when skin was exposed to both B[a]P and SSL than to B[a]P alone. We extended our work to a more realistic PAH exposure by using organic extracts of coal tar pitch. We used both raw organic extract and a synthetic mixture mimicking the PAH fraction. The same observations with B[a]P were made. These results indicate that UV significantly impairs B[a]P and PAH metabolism and decreases rather than increasing immediate toxicity. The time course observations made with B[a]P yet suggest that this phenomenon might be a delay rather than a complete reduction. It thus remains clearly established whether UV induced may decrease metabolism efficiency and may not change an acute exposure into a more chronic one as the result of an increased residence time of parent PAH in skin.

Figure: In workers, skin is often a common exposure route to PAH. The solar UV radiation may modulate the cutaneous response to these toxic compounds.

Recent Publications

1. Youssef A, Von Koschembahr A, Caillat S, Corre S, Galibert M D and Douki T (2019) 6-Formylindolo[3,2-b] carbazole (FICZ) is a very minor photoproduct of tryptophan at biologically relevant doses of UVB and simulated sunlight. Photochemistry and Photobiology 95 :237-243.
2. Bourgart E, Barbeau D, Marques M, Von Koschembahr A, Beal D, Persoons R, Leccia M T, Douki T and Maitre A (2019) A realistic human skin model to study benzo[a]pyrene cutaneous absorption in order to determine the most relevant biomarker for carcinogenic exposure. Arch Toxicol 93(1):81-93.

3. Von Koschembahr A, Youssef A, Beal D, Calissi C, Bourgart E, Marques M, Leccia M T, Giot J P, Maitre A and Douki T (2018) Solar simulated light exposure alters metabolization and genotoxicity induced by benzo[a] pyrene in human skin. Scientific Reports 8:14692.
4. Pollet M, Shaik S, Mescher M, Frauenstein K, Tigges J, Braun S A, Sondenheimer K, Kaveh, M, Bruhs A, Meller S, Homey B, Schwarz A, Esser C, Douki T, Vogel C F A, Krutmann J and Haarmann-Stemmann T (2018) The AHR represses nucleotide excision repair and apoptosis and contributes to UV-induced skin carcinogenesis. Cell Death and Differentiation 25:1823-1836.

Biography

Thierry Douki is a Senior Scientist interested in the genotoxic properties of several physical (UV radiation) and chemical agents (pollutants, warfare agents). Chemist by training, he is expert in the reactivity of DNA and uses HPLC-tandem mass spectrometry assays to quantify DNA damage in relevant cellular models. He is co-author of more than 250 articles and book chapters and is expert for the French Agency for Food, Environmental and Occupational Health & Safety (ANSES).

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