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In vitro assessment of the impact of cigarette smoke on skin

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ABSTRACT

Cigarette smoke stands among the most toxic environmental pollutants and is composed of thousands of chemicals including polycyclic aromatic hydrocarbons (PAHs). Despite restrict cigarette smoking ban in indoor or some outdoor locations, the risk of non-smokers to be exposed to environmental cigarette smoke is not yet eliminated. Beside the well-known effects of cigarette smoke to the respiratory and cardiovascular systems, a growing literature has shown during the last three decades its noxious effects also on cutaneous tissues. Being the largest organ as well as the interface between the outer environment and the body, human skin acts as a natural shield which is continuously exposed to harmful exogenous agents. Thus, a prolonged and/or repetitive exposure to significant levels of toxic smoke pollutants may have detrimental effects on the cutaneous tissue by disrupting the epidermal barrier function and by exacerbating inflammatory skin disorders (i.e. psoriasis, atopic dermatitis). With the development of very complex skin tissue models and sophisticated cigarette smoke exposure systems it has become important to better understand the toxicity pathways induced by smoke pollutants in more realistic laboratory conditions to find solutions for counteracting their effects. This doctoral thesis provides first a state of the art on the skin models currently available to study cigarette smoke exposure, the reported deleterious effects induced by CS in skin, as well as the inflammatory skin pathologies potentially induced and/or exacerbated by cigarette smoke exposure.

This study consists in investigating and providing further insight in the mechanical pathways involved in CS-induced toxicity in a 3D *in vitro* skin models, a well-characterized reconstructed human epidermis (RHE). As a first stage of the study, the reconstructed human epidermal model (RHE) will be fully characterized and validated as the main *in vitro* biological target, secondly it will focus on the implementation and optimization of the exposure conditions of cigarette smoke. Once both the skin model and the exposure conditions have been validated, markers of oxidative stress and inflammation can be assessed to relate pathways activated by the skin epithelial cells as a defense strategy against CS exposure. With this knowledge, therapeutic solutions may be developed targeting the altered markers, hence counteracting the detrimental impact. Finally, the reconstructed skin model was used to screen protective solutions against air pollutants such as cigarette smoke.