INFLAMMATORY SKIN DISEASES (OTHER THAN ATOPIC DERMATITIS & PSORIASIS)

INFLAMMAGING:INFLAMMASOME ACTIVATION ON SKIN EQUIVALENT

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Introduction: Inflammaging can be described as a chronic low-grade inflammation happening during human aging. It might be linked to a long-term activation of immune cells and a molecular misbalance and an increase of oxidative stress. Inflammaging and oxidative stress also correlates with an increase activation of the inflammasome complex. It can be activated in response to diverse stimuli recognized by pattern recognition receptors such as bacterial agents, neoplasia or environmental stress like UV exposure.

Objective: To better understand the role of inflammasome in inflammaging and be able to assess dermatological product mechanism of action, we aimed to develop an inflammaging model by focusing on UV light as an inducer of oxidative stress and inflammasome pathway.

Materials and methods: Bilayered reconstructed skin (T-Skin, Episkin) composed of epidermal and dermal compartments were slightly abraded and exposed to UVA and UVB (1 MED or 2 MED). Tissues were analyzed after 4h and 24h. Morphology was assessed by hematoxylin and eosin staining while specific immunostaining against NFκB and cleaved caspase-1 were performed. The secretion of IL-1β in response to UVR was assessed by ELISA.

Results: At 4h post irradiation, we observe an important nuclear translocation of NFκB with a dose-dependent effect relative to UV radiation. Cleaved caspase-1 level was increased in the superficial layer of the epidermis at 4h after irradiation, and at 24h the single increased in all the suprabasal layers of the epidermis indicating an activation of the inflammasome complex. Caspase-1 cleavage correlated with an increase in IL-1β secretion post-irradiation visible at 24h.

Conclusions: In vitro reconstructed skin has been demonstrated to be a reproducible, relevant and sensitive biological model to study inflammaging linked to UV-induced inflammasome. The mechanism based approach defined in this protocol can be applied to assess ingredients and dermatological products for their efficacy in a predictive human context.