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Effect of a psoriatic microenvironment in a three-dimensional model of normal human skin

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Among the cytokines involved in the pathogenesis and in the progression of the disease, tumor necrosis factor (TNF)-alpha and interleukin (IL)-17 are the most relevant. A three dimensional model of organotypic human skin cultures is a valuable approach for exposing the whole skin to TNF-alpha and IL-17 as specific proinflammatory stimuli, thus mimicking a psoriatic microenvironment. Normal human skin explants were obtained from plastic surgery of healthy 20-40 year-old women (n = 7) after informed consent. Bioptic fragments were cultured overnight in a DMEM medium and further divided before adding either 100 ng/ml TNF-alpha or 50 ng/ml IL-17 or a combination of both cytokines. Samples were harvested 24 hours after cytokine incubation. Each patient was represented in all experimental groups. Epidermal proliferation together with the expression of terminal differentiation biomarkers (keratin 10, K10, and 14, K14) and of intercellular adhesion (occludin for tight junctions and E-cadherin for adherens junctions) were investigated by indirect immunofluorescence.

Vibrational spectroscopy analysis by a confocal micro-Raman system (785nm laser) has been carried out in three skin samples to evaluate differences of the spectrum versus normal skin. Both cytokines induced a strong inhibition of keratinocyte proliferation (more than 80% compared with their respective controls). A non-continuous occludin expression in the granular layer was observed after the TNF-alpha and IL-17 exposure. Immunolabelings for E-cadherin in tight junctions, for K10 in the suprabasal layers, and for K14 in the basal layer were similar in all experimental groups.

The preliminary Raman results highlighted some biomolecules modifications in TNF-alpha- and IL-17-treated skin samples related to ceramide and amide III (keratin proteins) peaks.

These results suggest that in this experimental model we reproduced a psoriatic microenvironment in which TNF-alpha and IL-17 induce an early alteration of the homeostasis of the inner proliferative layer, the upper granular layer, and stratum corneum as shown by cell proliferation inhibition, occludin expression, and the biomolecules Raman bands.