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Structural and ultrastructural evaluation of the effects induced by IL-22 alone or in combination with psoriatic cytokines in an ex-vivo human skin model

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IL-22 is a pro-inflammatory cytokine playing a crucial role in the pathogenesis of psoriasis, an autoimmune chronic inflammatory skin disease. The immunological activation during the progression of the psoriatic lesion is driven by IL-22 together with other cytokines, such as (TNF)-alpha and interleukin (IL)-17 [1]. The aim of our study was to evaluate the early, direct, and specific effect of IL-22 alone or in combination with TNF-alpha and IL-17 by immunofluorescence on i) the molecular composition of intercellular junctions (desmocollin (DSC)1, E-cadherin, and occludin), ii) keratin(K) 10 and 17 expression, iii) keratinocyte proliferation, and, by transmission electron microscopy (TEM), on the ultrastructural morphology of the skin. An innovative model of human skin culture standardized in our laboratory, in which a psoriatic microenvironment was reproduced, was used [2]. Skin explants obtained from plastic surgery of healthy 20-40 year-old women (n = 7) after informed consent were cultured overnight in Dulbecco's modified Eagle's medium, divided before adding IL-22 or a combination of the three cytokines, and harvested 24, 48, and 72 hours after cytokine incubation.

Interestingly, keratinocyte proliferation was inhibited after exposure to the combination of cytokines while was not affected by IL-22 incubation. In both experimental groups, starting from T24, occludin immunostaining was non homogeneously distributed, K10 immunostaining gradually decreased in scattered clusters in the spinous layer, while K17 expression was induced and progressively increased with time in the suprabasal layers of epidermis. By TEM, after IL-22 incubation we observed keratin aggregates in the perinuclear cytoplasm of cells, while the combination of the three cytokines induced an enlargement of intercellular spaces.

Altogether, our results suggest that IL-22 mainly affects keratinocyte terminal differentiation, whereas, for inducing an impairment in cell proliferation, a more complex psoriatic-like microenvironment is needed.

References

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Keywords
Psoriasis; TEM; cytokines.