

Langerhans cells and Toll Like Receptors: how do they act and react in an in vitro psoriatic microenvironment?

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Tumor Necrosis Factor (TNF)- α , interleukin (IL)-17, IL-22 and IL-23 are involved in the psoriasis pathogenesis and represent a strong proinflammatory stimulus. Both epidermal keratinocytes (KCs) and Langerhans cells (LCs) early respond promoting an early epidermal response [1, 2]. Human skin can count on the cellular response supported by LCs and on innate immunity through the expression of Toll-like Receptors (TLRs) [4]. We aimed at investigate whether the exposure of normal human skin to a combination of TNF- α , IL-17, IL-22, and IL-23 (cytokine mix) affected i) LCs immunophenotype, ii) expression of TLR2 and TLR9 and iii) KC proliferation. Human skin samples were obtained after plastic surgery (n = 5) and exposed to the cytokine mix in a Transwell system at air-liquid interface, with a parallel control group. Samples were harvested 24 and 48 hours after cytokine stimulation, processed in parallel for immunofluorescence or ultrastructural analysis. A decrease of cell proliferation was evident in samples exposed to cytokine mix for 24 hours and this phenomenon was more and more evident later. TLR2 immunopositivity progressively disappeared in the basal layer after cytokine mix exposure compared to the control group, while TLR9 expression was induced in scattered granular keratinocytes. By TEM, LCs showed an activated phenotype. In conclusion, these results suggest that, in a microenvironment mimicking the psoriatic plaque, epidermis early stimulates two important lines of defense, thus proposing that a therapeutic intervention in this direction can interfere with the formation/progression of the psoriatic plaque.

References

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Keywords

Human epidermis; transmission electron microscopy; cell proliferation; cell differentiation.