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Morphological correlation between Psoriasis Vulgaris and Guttate and a 3D in vistro psoriatic microenvironment

Laura Cornaghi[1], Giulia Lombardo[1], Elena Donetti[1] and Francesca Prignano[2]

[1] Università degli Studi di Milano, Department of Biomedical Sciences for Health, Milan, Italia
[2] Università degli Studi di Firenze, Department of Surgery and Translational Medicine, Florence, Italia

Psoriasis is characterized by a great variety of clinical manifestations and they vary according to different phenotypes. Guttate or eruptive psoriasis (PG) [1] shares genetic similarities with psoriasis vulgaris (PV) [2], the most represented clinical form. Cell types and molecules of both the innate and adaptive immunosystem are involved in the pathogenesis/progression of the disease, but several data concerning the early phase of the disease lack. A three dimensional model of organotypic cultures of normal human skin biopsies represents an useful approach for investigating the cellular mechanism(s) involved in the early epidermal response to proinflammatory psoriatic cytokines [3;4]. The aim of this study was to compare cellular proliferation, the expression of Toll-like receptors (TLR) 7 and 9, and the innate immune response in lesional and perilesional skin of patients affected by PV or PG and in our model of organotypic culture after exposure to a cytokine mix (IL-17, IL-22, IL-23, and TNF-alpha) in a time-course study. Parallel ultrastructural analysis was performed. Keratinocyte proliferation in non lesional skin of both PG and PV was comparable, with PV lesional area as the most proliferative. In PG cell proliferation was exclusively localized in the basal layer. After mix incubation, a progressive decrease of cell proliferation was detected as an early response to proinflammatory stimulus. TLR9 was present in the granular layer of non lesional skin and mix samples and in the suprabasal layers of PV/PG lesional skin. TLR7 distribution was clearly different in each group, highlighting a specific response to the specific microenvironment.

In conclusion, these results prove that a psoriatic microenvironment is able to modify the expression of TLR7 and TLR9 in our model from human skin. These observations provide also new insights regarding the specific localisation of these two receptors and this could be an important detail for the many new small molecules targeted against TLRs for the therapy of chronic inflammatory disease, including psoriasis.

References

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Key words

Cytokine, keratinocyte proliferation, Toll-like receptors.

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