

Morphological features induced by interleukin 17 in a 3D organotypic cultures of normal human skin are promptly reverted by a specific biological inhibitor

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Psoriatic plaque is the result of a strict interaction among epidermal cells, immune system, and soluble cytokines. Interleukin 17 (IL-17) is a well-known proinflammatory psoriatic cytokine mainly produced by the T helper subclass Th17. In the last decade we standardized a 3D model organotypic cultures of normal human skin for studying the early, intrinsic and specific effects induced by IL-17. We demonstrated that IL-17 elicited Langerhans cell (LC) activation and migration, keratin 17 expression, Toll like receptor 7 and 9 expressions and profoundly altered filaggrin expression, without affecting the suprabasal distribution of keratin 10 and keratin 14. Moreover, this cytokine early inhibited keratinocyte proliferation, strongly suggesting that this event can be the basis for the response to injury leading to the psoriatic characteristic hyperproliferation observed in lesional plaques. In the present study, we incubated bioptic skin fragments obtained after aesthetic surgery of healthy young women (n=5) with i) IL-17 alone, ii) with a combination of IL-17 and an IL-17 biological inhibitor, iii) with the IL-17 biological inhibitor alone. Control samples were in parallel cultured. Incubation lasted for 24 and 48 hours with skin at the air-liquid interface. Immunofluorescence experiments and transmission electron microscopy (TEM) analysis were carried out. Samples incubated with the IL-17 biological inhibitor were comparable to controls. By immunofluorescence, the combination reverted IL-17-induced effects at all considered time-points. By TEM, LCs appeared less activated as shown by the paucity of Birbeck granules and the highly dispersed nuclear chromatin. The epidermal ultrastructure was comparable in all groups, with well-preserved desmosomes, interspersed keratin filaments and terminally differentiated granular keratinocytes/corneocytes. These results highlight the clinical usefulness of this experimental approach for identifying the early psoriatic processes that can be modulated by last generation biological agents.