PSORIASIS

INTERLEUKIN-22 AND SKIN: FROM EPIDERMAL HOMOESTASIS TO PSORIASIS

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Interleukin-22 (IL-22) together with the IL-10 receptor b (IL-10Rb) and the IL-22 receptor (IL-22R) are expressed by epithelial cells. In humans it is released by cells of the adaptive and innate immune system. The IL-22–IL-22R pathway has been shown to modulate the expression of many genes encoding proteins involved in tissue protection, survival, differentiation, and remodeling, and to a lesser extent pro-inflammatory proteins. IL-22 enhances the release of metalloproteinases (MMPs), with migration of immune cells to the site of inflammation by inducing proteolytic degeneration of collagens and proteoglycans. IL-22 promotes chemokines expression by keratinocytes; activates the STAT-3 pathway, affects the proliferation and differentiation of keratinocytes. In keratinocytes, IL-22 dose dependently reduces the expression of the differentiation-associated proteins: profilaggrin, keratin1, keratin 10, and kallikrein 7, which regulate the terminal differentiation and promote keratinocyte proliferation. Th22 cells are elevated in psoriatic patients and accumulate in lesional psoriatic skin. In our standardized 3D model organotypic cultures of normal human skin, reproducing early psoriatic microenvironment, IL-22 treated samples showed a progressive decrease in K10 immunostaining paralleled by K17 induction. By TEM keratin aggregates were evident in the perinuclear area. Occludin immunostaining was not homogeneously distributed. Conversely, keratinocytes proliferation was not inhibited by IL-22 alone, but only by the combination of many cytokines. These results together with the data of the literature suggest that IL-22 affects keratinocyte terminal differentiation, whereas, in order to induce a proliferation impairment, a more complex psoriatic-like microenvironment is needed. While TNF-alpha and IL-17 inhibitors have been widely used in many trials and in clinical practice to treat psoriasis, the relevance of IL-22 has not been explored yet.