Psoriasis

The skin constitutes the largest physical and chemical barrier against various stresses including pathogens, constituting the first line of defense of the body. Cutaneous homeostasis and defenses are maintained by permanent cross-talk among dermal fibroblasts, epidermal keratinocytes, and cells of the immune system residing or recruited in the skin, through the production of cytokines. The skin represents a very attractive tissue that is a paradigm for studying the cross-talk between innate and adaptive immune system and an organ. If required, a coordinated inflammatory response is triggered, relayed by specific cytokines. Due to the action of the cytokines released together with the environmental conditions and the genetic background a chronic inflammation enclosed in a vitreous circle can be induced. This crosstalk between T cells and keratinocytes in a 3D microenvironment This type of crosstalk is an essential feature in disease pathogenesis, as immune cells produce mediators to activate keratinocytes that in turn modulate the expression of skin-homing markers on T cell and produce chemokines to attract immune cells thereby completing the vicious circle of chronic inflammation [1-4]. This state is characterized by resident/infiltrating immune cells in the epidermis or dermis, and altered differentiation of keratinocytes.

To clarify the Physiopathology of Chronic Atopic Dermatitis and Psoriasis Bernard et al. designed in vitro experiments aiming to culture normal human epidermal keratinocytes (NHEK) and reconstituted human epidermis (RHE) with a mixture of IL-22, TNF?, IL-4, and IL-13 or an alternative mixture of IL-22, TNF?, and IL-17, with the objective to, respectively, mimic AD and psoriasis epidermis. In these models, we finally analyzed the effects of the change from IL-17 (Th17, psoriasis) to IL-4/IL-13 (Th2, AD), in the same cytokine background (TNF? and IL-22). Most of the so-called epidermis differentiation markers are down regulated in NHEK by both AD and PSO NHEK treatments, as observed in pathologic skin. (PSO) when compared to the weak enhancement induced by the IL-4/IL-13-containing mix (AD).

The results parallel the in vivo situation, in which psoriatic skin is characterized by high expression levels of these antimicrobial peptides, functionally associated to a large degree of resistance to infections in psoriasis, and exacerbated infection sensitivity in AD skin.
Psoriasis is regarded as a mixed Th1/Th17 disease as products of these cells dominate the cytokine network in psoriasis and drive the keratinocyte hyperproliferation and skin inflammation characteristic of this disease. IL19 has been proposed as a biomarker for psoriasis disease activity [85]. The authors’ demonstrate that the up regulation of Il19 expression in psoriatic skin is driven by IL17A. The cutaneous IL-19 overproduction was reflected by elevated IL-19 blood levels that correlated with psoriasis severity [5]. IL-19 appears to have similar but much weaker effects on keratinocytes compared with IL-22 [6]. However, given its more abundant expression, IL-19 may be a significant part of the cytokine network in that it can amplify the effects of IL-17A and promote the IL-23/IL-17 inflammatory axis [5]. Between IL17 and TNF? there are potent synergistic effects in the IL-17 stabilization and the expression of receptors for IL-17 and TNF? by keratinocytes [7]. IL-17 plays a key role in host defense against certain pathogens through stimulating the release of antimicrobial peptides and pro-inflammatory cytokines and chemokines. The increased expression of IL-17A at sites of inflammation in psoriasis [8, 9] as well as other autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, and Crohn’s disease strongly suggests a role in promoting autoimmune pathology. [7].

Table 1: Cytokines (column 1) in the psoriasis network leading to the known hyperproliferation of keratinocytes mediated by T-helper cell functions (Column 3) (summarized from [5, 7, 10]).

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