Psoriasin exacerbated inflammation effects in response to IL17 in human keratinocyte cells through NLRP3-inflammasome pathway.

Chih-Tsung Hung [1], Zhao-Yin Chen[2], Yung-Lung Chang[2], Wei-Ming Wang[1]
[1]Department of Dermatology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan; [2]Department of Biochemistry, National Defense Medical Center , Taipei, Taiwan

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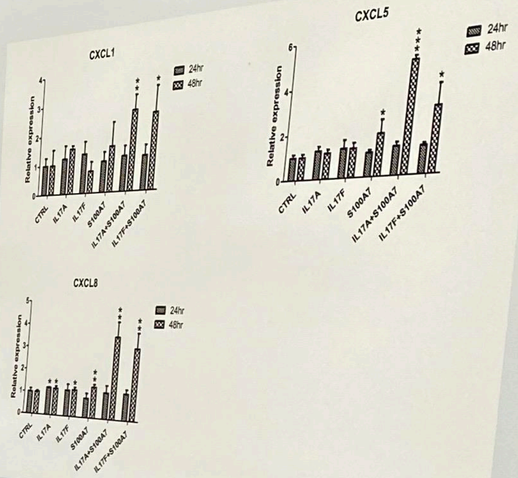
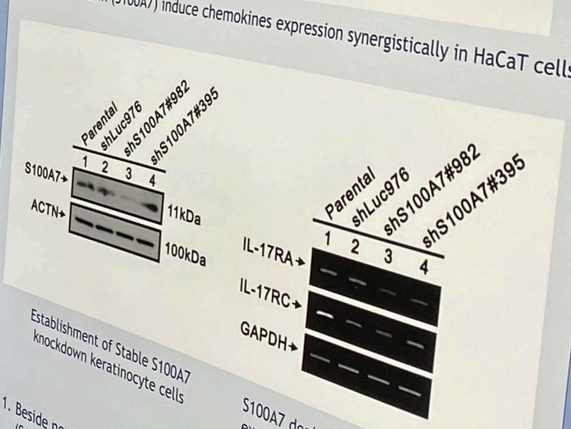
Introduction

Psoriasis is a chronic inflammatory disorder. The skin rash presents with scaly, erythematous papules, patches, or plaques clinically. In Taiwan, it affects approximately 0.23% of the population. Besides, psoriasis is more than "skin deep", as the hypertension, hyperglyceridaemia, diabetes, heart disease, and autoimmune diseases are associated with psoriasis. The pathogenesis of psoriasis is quite complicated, and it involves the genetic factors, innate and adaptive immune systems. Innate immune cells, as nature killer T cells, plasmacytoid dendritic cells and macrophages, secrete cytokines, for instance tumor necrosis factor α (TNF-α), interleukin-1β, and interleukin-6 etc, that activate myeloid dendritic cells. Activated dendritic cells produce mediators, such as interleukin-12 (IL)-12 and IL-23, that induce the differentiation of type 1 and type 17 helper T cells (Th1 and Th17). The activated T cells release several cytokines, augment the inflammation, and stimulate keratinocytes proliferation and dedifferentiation. Several studies reveal that Th17 cells play an important role in the psoriasis. Comparing with the non-lesion sites, increased numbers of cutaneous Th17 cells accumulate in the lesion sites. Th17 cells produce several cytokines, including IL17A, IL17F, IL21 and IL22. Among them, IL-17 induces the expression of neutrophil chemoattractants CXCL1, CXCL3, CXCL5, and CXCL6. Although the importance of IL-17 in psoriasis is confirmed by the effective treatments targeting either the IL-17 cytokine (i.e. Secukinumab) or blocking the IL-17R (i.e. Broadalumab), the role of psoriasin secreted by keratinocytes in response to [illegible] unknown.

Results (Cont.)



IL17 and psoriasin (S100A7) induce chemokines expression synergistically in HaCaT cells



Establishment of Stable S100A7 knockdown keratinocyte cells

S100A7 depletion suppressed the gene expression of the IL-17 receptors

Conclusion

1. Beside neutralizing IL-17 cytokine or blocking IL-17R, targeting psoriasin (S100A7) may be an appealing strategy for psoriasis treatment.
2. The receptor of psoriasin (S100A7) remains elusive and worth for further investigation.
3. Dysregulation of IL-17 in the lesions of psoriasis microenviroment could be chronically augmented by psoriasin (S100A7).