PSORIASIS

CD8+CD69+ TRM CELLS HOLD IMMUNOLOGICAL MEMORY BY IL-15 IN PSORIATIC RECURRENCE

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Introduction: One of the major therapeutic challenges of plaque psoriasis is its frequent recurrence, which is preferentially in previously affected areas. Thus, a pathogenic memory has been proposed, however, the nature of such site-specific immuno-memory is not well known. Because tissue resident memory T cells (TRM cells) can localize and survival in peripheral compartments for many months, even years, we speculate that TRM cells may contribute to the recurring pathology of psoriasis.

Objective: To explore the role of TRM cells in psoriasis recurrence and the cytokine(s) responsible for their long-term survival.

Materials and Methods: Psoriatic recurrence was investigated by questionnaires. RNA-seq analysis was performed among recurrent lesions, resolved areas, and adjacent "appearing" normal skin. CD8+CD69+ TRM cells were evaluated quantitatively, and their function was demonstrated by ex vivo stimulation and re-activate mouse psoriasiform dermatitis. IL-15's function on CD69 was evaluated on cell level. The cooperation of MTX and anti-IL-15 mAb was demonstrated by organ culture of psoriatic lesions.

Results: About 94% psoriatic patients experienced the recurrence in previously affected areas. We demonstrated dermal CD8+CD69+ TRM cells existed with high numbers in resolved areas, and could secret pathogenic cytokines upon stimulations. IL-15 was secreted by psoriatic keratinocytes under experimental Koebner stimulations (bending & stretching of keratinocyte, wound trauma), and maintained a high level in clinically resolved areas. We demonstrated IL-15 was important for CD69 maintenance, and indispensable for the survival of CD8+CD69+ TRM cells. Although MTX failed, MTX plus neutralizing anti-IL-15 mAb could decrease CD8+CD69+ TRM cells in resolved areas.

Conclusions: We demonstrated the vital roles of the immunological memory of dermal CD8+CD69+ TRM cells by IL-15 in psoriatic recurrenc. Our results suggest a novel potential therapeutic strategy for decreasing psoriasis recurrence, in which IL-15 antagonist(s) targeting at CD8+CD69+ TRM cells may be an important supplement to

routine therapeutic regimens.