The Editor's Choice

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Anti-IL-17A and IL-23p19 antibodies but not anti-TNFα antibody induce expansion of regulatory T cells and restoration of their suppressive function in imiquimod induced psoriasiform dermatitis

Anti-TNFα, IL-17A and IL-23p19 antibodies are effective for psoriasis. However, the contribution of regulatory T cells (Treg) in their effectiveness remains to be elucidated. Shimizu T et al investigated the effects of TNFα, IL-17A and IL-23p19 inhibition on Tregs in imiquimod-induced psoriasiform dermatitis. Administration of anti-TNFα, IL-17A or IL-23p19 antibodies improved the clinical score and downregulated Th17-related cytokines and chemokines, while IL-23p19 antibodies upregulated IL-10 mRNA expression. Anti-IL-17A or IL-23p19 antibody-treated imiquimod applied mice showed a significant increase in the number of Tregs. Recipient mice adoptively transferred with Tregs derived from donor mice treated with antibodies demonstrated clinical and pathological improvement in imiquimod-induced psoriasiform dermatitis. Anti-IL-17A or IL-23p19 antibody-induced Tregs significantly increased the number of Foxp3+ cells and IL-10 expression in imiquimod-induced psoriasiform dermatitis in recipient mice but anti-TNFα antibody-induced Tregs did not. Anti-IL-17A or IL-23p19 antibody inhibits the IL-17/IL-23 signaling pathway, and induces expansion of Tregs and their suppressive capacity in imiquimod-induced psoriasiform dermatitis.

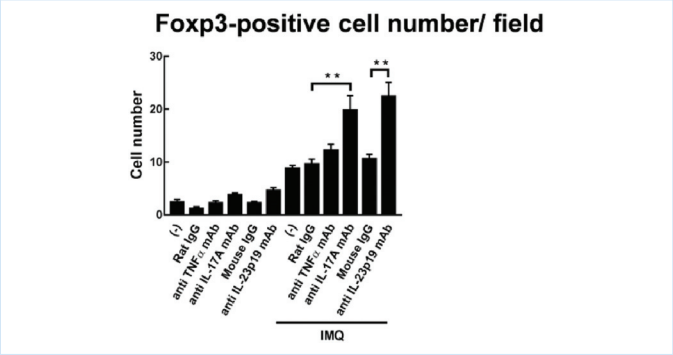

Fig. 3. Foxp3⁺ cell infiltration in IMQ-induced psoriasiform skin of mice injected with anti-cytokines mAb or control IgG. (B) The Foxp3⁺-infiltrating dermal inflammatory cells were counted in five random grids per section under x400 high-power field. The data are shown as mean ± SEM of samples pooled from three independent experiments. In each experiment, each group contained two mice (n = 6). ** $p < 0.01$ (ANOVA with Bonferroni's post-test).

Thimerosal induces skin pseudo-allergic reaction via Mas-related G-protein coupled receptor B2

Thimerosal has been used as a preservative in many products which may cause contact dermatitis, which is generally considered to be a delayed-type hypersensitivity reaction, but it is difficult to explain the fact that most patients develop an allergic reaction upon first encounter with thimerosal. Recent studies have demonstrated the association between Mas-related G protein coupled receptor X2 (MRGPRX2) and pseudo-allergic reactions. Peng B et al investigated the role of Mas-related G-protein coupled receptor B2 (MrgprB2)/MRGPRX2 in contact dermatitis induced by thimerosal. Thimerosal induced contact dermatitis in wild-type mice, but had no significant effect in MrgprB2-knockout mice. Thimerosal-induced dermatitis is characterized by infiltration of inflammatory cells and elevation of serum histamine and inflammatory cytokines, rather than elevation of serum IgE level. Thimerosal increased the intracellular Ca2+ concentration in HEK293 cells overexpressing MrgprB2/MRGPRX2. MrgprB2 mediates thimerosal-induced mast cell degranulation and pseudo-allergic reaction in mice. MRGPRX2 may be a key contributor to human contact dermatitis.

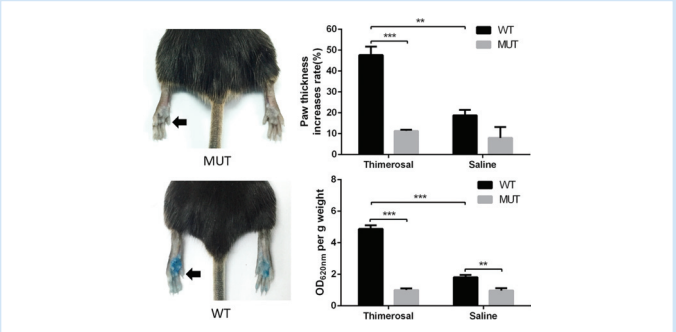

Fig. 3. MrgprB2 mediated pseudo-allergic reaction induced by thimerosal. $kit^{W-sh}/^{W-sh}$ mice and MrgprB2-/- (MUT) mice were injected with 5 μg/ml of thimerosal in the left paw (arrowhead) and saline was administered in the right paw as a negative control, 30 μg/ml C48/80 as positive control. (B) Thimerosal could not induce pseudo-allergic reaction in MrgprB2-/- (MUT) mice. (n = 6 per genotype).

Decreased expression of suprabasin induces aberrant differentiation and apoptosis of epidermal keratinocytes: Possible role for atopic dermatitis

Suprabasin (SBSN), a secreted protein, is expressed in various epithelial tissues. The role of SBSN in epidermal differentiation and atopic dermatitis (AD) pathology remains largely unknown. Aoshima M et al evaluated the effects of SBSN on epidermal keratinocytes and its role in AD. Epidermal SBSN expression was decreased in AD lesional skin compared to healthy skin. The SBSN serum levels were significantly lower in AD patients than in normal subjects. The SBSN-deficient three-dimensional human living skin equivalent (LSE) exhibited compact stratum corneum, immature stratum granulosum, and increased keratinocyte apoptosis. The cytokines did not affect SBSN expression in LSE. SBSN deficiency-induced apoptosis of keratinocytes was exaggerated by IL-4/IL-13. These data demonstrated that SBSN regulates normal epidermal barrier. The cytokines unaffect SBSN expression in keratinocytes, but promote SBSN deficiency induced apoptosis. It is suggested that SBSN has an anti-apoptotic activity, and its deficiency is involved in the pathogenesis of AD.

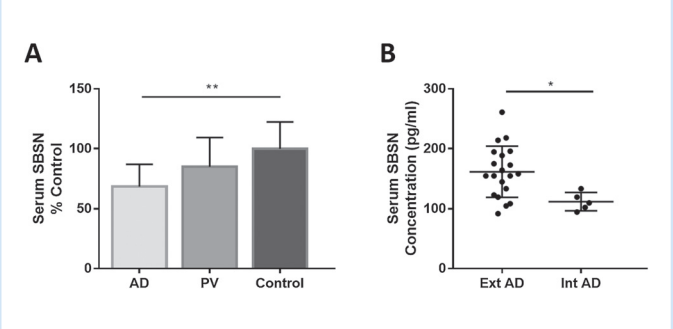

Fig. 2. Significantly lower SBSN serum levels in AD patients than in healthy individuals. (A) SBSN serum level were measured by ELISA in AD patients (n = 13; SCORAD 39.5 ± 20.5), psoriasis vulgaris (PV) patients (n = 12), and healthy control (n = 9). **$P < 0.01$. (B) SBSN serum levels were measured by ELISA in intrinsic AD (Int AD; n = 5, SCORAD; 41 ±17), extrinsic AD (Ext AD; n = 20, SCORAD; 51 ± 18). *$P < 0.05$.