The Editor's Choice

Abe R

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COA-Cl prevented TGF-β1-induced CTGF expression by Akt dephosphorylation in normal human dermal fibroblasts, and it attenuated skin fibrosis in mice models of systemic sclerosis

Systemic sclerosis (SSc) is characterized by fibrosis of the skin and internal organs. Although TGF-β1-induced CTGF expression has been presented in SSc fibrosis, the therapeutic potential of targeting CTGF in SSc has not been fully explored. COA-Cl is a novel nucleic acid analog, which is reported to have pleiotropic beneficial biologic effects. Nakai K et al showed COA-Cl attenuated the TGF-β1-induced expression of both CTGF mRNA and protein. Although COA-Cl did not alter the TGF-β1-induced phosphorylation of Smad2/3 or ERK1/2, it reduced the TGF-β1-induced phosphorylation levels of Akt. Notably, COA-Cl dephosphorylated the Akt of lysates of TGF-β1-treated fibroblast. COA-Cl reduced the levels of CTGF mRNA, CTGF protein, dermal thickness, collagen content and Akt phosphorylation in the skin of mice SSc model. These results imply that the inhibition of TGF-β1-induced CTGF expression by COA-Cl may be a therapeutic approach for SSc.

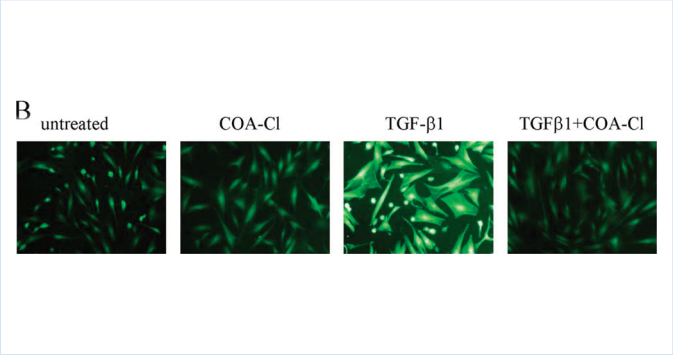

Fig. 4. COA-Cl attenuated the TGF-β1-induced ROS formation in NHDF. The ROS formation was assessed by DCF staining. **(B)** Representative fluorescence microscopic images at ×400 were shown.

Identification of genetic alterations in extramammary Paget disease using whole exome analysis

Extramammary Paget disease (EMPD) is a rare cutaneous malignant neoplasm, and the genomic alterations underlying its pathogenesis are unknown. Kniwa Y et al aimed to identifytumor-specific genomic alterations in EMPD. Exome analysis revealed recurrent somatic mutations in several genes, includingTP53, PIK3CA, and ERBB2. They identified additional candidate exons by searching the COSMIC database for exons that are frequently mutated in other adenocarcinomas. They obtained 19 exons in 12 genes as candidate exons, and performed target amplicon sequencing in samples obtained from EMPD patients. New somatic mutations in the TP53 gene were identified in six EMPD patients. Single nucleotide polymorphism analysis revealed multiple chromosomal alterations in three EMPD specimens, and two specimens exhibited amplification of chromosome 12p13 and losses of 3p21–24, 7q22 and 13q12–21. This comprehensive genetic analysis identified novel genomic alterations, and will inform treatment options for EMPD.

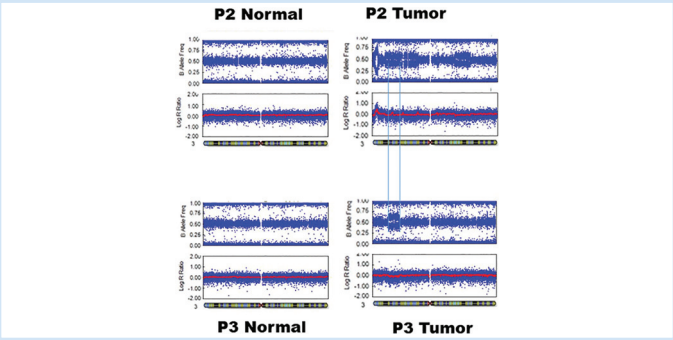

Fig. 1. (C) Chromosomal copy number alterations inextramammary Paget disease. Left panels: Copynumber alterations in chromosome 3 of P2 and P3. Chromosome 3p shows deletions in tumor samples. B allele frequencies and log R ratio are indicated in the upper and lower parts of each panel, respectively.

Cyto/chemokine profile of in vitro scratched keratinocyte model: Implications of significant upregulation of CCL20, CXCL8 and IL36G in Koebner phenomenon

Scratch injury induces Koebner phenomenon in psoriasis. Keratinocytes can produce various psoriasis-related molecules, however, the scratch-induced molecular profiling remains elusive. Furue K et al aim to profile the induction pattern of above-mentioned psoriasis-related and keratinocyte-derived molecules by scratch injury. Among the 18 molecules, the scratch injury on a confluent keratinocyte sheet significantly and selectively upregulated the mRNA expression of four cyto/chemokines, CXCL8, CCL20, IL36G, and TNF, in a scratch-line-number-dependent manner under either low- or high-calcium condition. However, significant protein secretion was only demonstrated for CXCL8 and CCL20. The IL36 G protein was not secreted, but its intracellular level was significantly upregulated by scratch injury, whereas neither the secretion nor the intracellular level of TNF protein was affected by scratch injury. Dexamethasone, but not maxacalcitol nor the phosphodiesterase 4 inhibitor apremilast, partially inhibited the CXCL8 and CCL20 secretion. CCL20 and to a less extent CXCL8 may play a key role in triggering the Koebner phenomenon after scratch injury to keratinocytes.

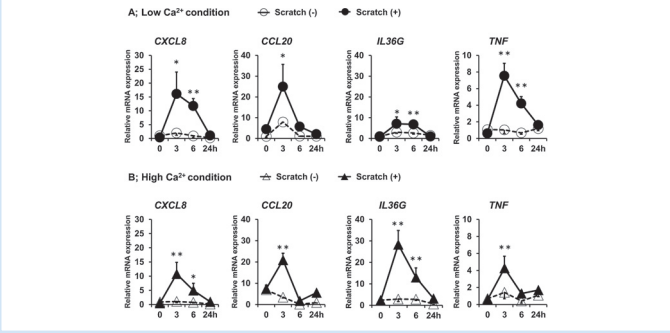

Fig. 1. Gene expression of *TNF, IL36G, CXCL8,* and *CCL20* was significantly upregulated in scratch(+) keratinocyte sheet (closed circle and closed triangle) compared with scratch(−) control sheet (open circle and open triangle). A: Low-Ca^{2+} conditions. B: High-Ca^{2+} conditions. Each experiment was performed in triplicate. (N = 5. Normalized against *ACTB* expression).
*: $P < 0.05$ and **: $P < 0.01$ compared with scratch(−) control.