Impaired function of ECM1 underlies the pathogenic disorganization of vascular and basement membrane molecules in lichen sclerosus

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Tissue fibrosis is one of the major causes of CSU. The reported prevalences of IgG autoantibodies (AAbs) to FcRI have varied, and these AAbs are also often observed in healthy control subjects. Thus, we sought to determine the prevalence and FcRI crosslinking, as compared to anti-FcRI AAbs and the abilities of these AAbs to cause FcRI aggregation in patients with CSU and healthy control subjects. The results indicate that cellular activity is lower at lower temperature. However, when gene expression was examined under conditions of in vitro experiments when extrapolating to in vivo.

Inhibitory effect of kaempferol on skin fibrosis in systemic sclerosis by the suppression of oxidative stress

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Kaempferol is a natural flavonoid widely found in various vegetables and fruits, and has been reported to have excellent antioxidant activity. Objective was to elucidate the effect of kaempferol on skin fibrosis and the mechanism of the inhibition of regulatory fibroblasts by kaempferol. We assessed the effect of intra-peritoneally administered kaempferol on bleomycin-induced dermal fibrosis in mice. The effect of kaempferol on oxidative stress in bleomycin-treated mice and SSc fibroblasts was assessed in vitro. We identified that kaempferol injection significantly inhibited bleomycin-induced dermal fibrosis in mice. The number of SAα1 smooth fibroblasts, CD3+ T cells, and CD66+b macrophages in lesional skin was significantly decreased by kaempferol injections. Kaempferol administration also significantly suppressed the bleomycin-induced oxidative stress signal in OKD4 mice. Additionally, mRNA levels of oxidative stress-associated factors, such as HO-1 and NOX2, as well as inflammatory and pro-fibrotic cytokines, including IL-6, TGF-β and TNFα in sclerotic skin were significantly decreased by kaempferol. Kaempferol also reduced bleomycin-induced TUNEL+ apoptotic cells in the lesional skin of SSc fibroblasts by siRNA-knockdown for ECM1 and analyzed transcription profiles by cDNA microarray. Comparison with siRNA-untransfected fibroblasts identified 3,015 differentially expressed genes. Functional assessment assigned that 1,477 upregulated and 1,564 downregulated genes are related to proteins binding to DNA, post-translational modifications, extracellular components, enzymes and growth factors facilitating fibroblast proliferation, contributing to the lesional skin pathology.

Th17 induction of IL-10-producing plasmablasts during contact hypersensitivity

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Th17 cells, which are involved in the blockage of B cell maturation and the delayed reappearance of Dsg+ memory TFH cells was much lower in patients treated with RTX than in those treated with CS. Our study demonstrated that the concentration of anti-IgE AAbs was significantly different between the NC subjects and the CS patients (P < 0.0001, cutoff value: 0.558 µg/mL), whereas the concentration of anti-FcRI AAbs was not. A significant difference in the duration of illness was noted between patients with lower and those with higher concentrations of anti-IgE AAbs relative to the cutoff value. The ability of anti-IgE AAbs, but not anti-FcRI AAbs, to induce FcRI crosslinking was significantly higher in NC subjects than in SSc patients (P = 0.0106). In the Japanese population of CSU patients studied, the ability of the anti-IgE AAbs to induce FcRI crosslinking differed significantly between NC subjects and CS patients, suggesting the involvement of anti-IgE AAbs in the pathogenesis of CSU in the Japanese population.

Evolution of autoreactive B and T cells in pemphigus patients with Rituximab or corticosteroid regimen treatment

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Fifteen pemphigus patients (11 Pemphigus vulgaris, 4 Pemphigus foliaceus) were included in this study. In CR patients, RTX induced a significant decrease of IgG switched memory Dsg+ B cells. Our study demonstrated that the concentration of anti-IgE AAbs in the lesional skin of SSc fibroblasts was inhibited by kaempferol treatment. In addition, the oxidant-induced apoptosis of SSc fibroblasts was decreased by kaempferol in vitro. Kaempferol might improve bleomycin-induced fibrosis by reducing oxidative stress, inflammation, and oxidative cellular damage. Administration of kaempferol might be an alternative treatment for skin fibrosis in SSc.

Phenotypic Changes of a Monocyte Cell Line under the Culture Temperature

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Monocytes are terminally differentiated cells that originate from hematopoietic progenitors and are involved in the adaptive immune response. However, the impact of temperature on monocyte function is not fully understood. The present study investigated the phenotypic and functional changes of a human monocyte cell line (THP-1) at different temperatures. THP-1 cells were maintained at 37°C, the temperature of skin, which is facing directly to external environment, is affected by external climate. Since epidermal Langerhans cells reside in uppermost layers of skin, they must be affected with temperature shift. However, the immunological effects of Langerhans cells were examined using a model cell line, THP-1 cells. Since the skin surface temperature goes down to 25°C when people go to a room at 10°C, we chose the culture temperature at 29°C, 31°C, and regular 37°C. The proliferation rate declined as temperature went down. The amount of RNA extracted from the same number of cells cultured at lower temperature was smaller than at 37°C. These results suggest that cellular activity is lower at lower temperature. However, when gene expression was examined under conditions of in vitro experiments when extrapolating to in vivo.

Differential between control subjects and patients with chronic spontaneous urticaria based on the ability of anti-IgE autoantibodies to induce FcεRI crosslinking, as compared to anti-FcγRII AAbs

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The reported prevalences of IgG autoantibodies to FcεRI and IgE in sera from patients with CSU have varied, and these AAbs are also often observed in healthy control subjects. Thus, we sought to determine the prevalence and FcεRI crosslinking ability of these AAbs in a large number of patients with CSU and nonatopic control (NC) subjects. Our experiments were designed to compare the concentrations of anti-IgE and anti-FcεRI AAbs and the abilities of these AAbs to cause FcεRI aggregation in patients with CSU (n = 34) and NC subjects (n = 55) using ELISA and an in vitro elicitation test, respectively. Our study demonstrated that the concentration of anti-IgE AAbs was significantly different between the NC subjects and the CS patients (P < 0.0001, cutoff value: 0.558 µg/mL), whereas the concentration of anti-FcεRI AAbs was not. A significant difference in the duration of illness was noted between patients with lower and those with higher concentrations of anti-IgE AAbs relative to the cutoff value. The ability of anti-IgE AAbs, but not anti-FcεRI AAbs, to induce FcεRI crosslinking was significantly higher in NC subjects than in SSc patients (P = 0.0106). In the Japanese population of CSU patients studied, the ability of the anti-IgE AAbs to induce FcεRI crosslinking differed significantly between NC subjects and CS patients, suggesting the involvement of anti-IgE AAbs in the pathogenesis of CSU in the Japanese population.