001

Ginsenoside compound K ameliorates the severity of imiquimod-induced psoriatic pathology by inhibiting REG3A/RegIIIγ in mice

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Psoriasis is a chronic inflammatory skin disease. Ginsenoside compound K (CK) is an active ingredient of ginseng which is reported to exert beneficial effects on inflammation. However, the biological role of ginsenoside CK in psoriasis is still unclear. Our aim was to investigate the effect of ginsenoside CK on the proliferation of keratinocytes and the expression of human regenerating islet-derived protein 3A (REG3A) and its mouse homolog RegIIIγ as well as the inhibitory effect of ginsenoside CK on IMQ-induced psoriasis-like mice. The effect of ginsenoside CK on the proliferation of HaCaT cells and NHEK cells was measured by MTT. The apoptosis of HaCaT cells induced by ginsenoside CK was analyzed by flow cytometry. The inhibitory effect of ginsenoside CK on RAG3A induced by IL-36γ in HaCaT cells was identified by WB and qRT-PCR. Psoriatic models in mice were induced by imiquimod cream. The thickness of mouse ear and skin epidermis was measured based on hematoxylin and eosin stain (HE) of tissues. The expression of RegIIIγ protein in lesional skin of psoriatic mice was identified by WB and immunofluorescence. Ginsenoside CK could inhibit the proliferation of HaCaT cells and NHEK cells, but it could not induce the apoptosis of HaCaT cells. The expression of RAG3A protein stimulated by IL-36γ is inhibited by ginsenoside CK in HaCaT cells. In the mouse model of psoriasis, the topical application of ginsenoside CK significantly decreased the epidermis thickness of lesional skin of psoriatic mice and the expression of RegIIIγ protein. Ginsenoside CK inhibited the proliferation of HaCaT cells and NHEK cells as well as attenuated imiquimod-induced psoriasis-like pathology in mice by reducing the expression of RAG3A/RegIIIγ protein. These results indicated that ginsenoside CK exhibited therapeutic effects in psoriasis.

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RNA-seq analysis reveals unique transcriptome signatures in dermatomyositis with distinct autoantibodies specificities

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To investigate the transcriptional difference between dermatomyositis with distinct autoantibodies. we performed high throughput sequencing technologies in 27 dermatomyositis and 7 healthy volunteers. These dermatomyositis patients were segregated into three subsets based on distinct autoantibodies present in their sera. Including 10 patients that anti-melanoma differentiation associated gene 5 antibody (MDA-5) positive with interstitial lung disease (ILD, and 8 patients that anti-transcriptional intermediary factor 1-γ(TIF1-γ) antibody positive with tumor, and 9 patients that both two antibodies are negative with neither interstitial lung disease nor tumor. We extract RNA from the peripheral blood mononuclear cells of these patients and healthy controls. BGI-seq 500 RS was using for sequencing. Gene ontology analysis and pathway enrichment analysis revealed cytokine activity, receptor binding and protein binding molecular function were specifically dysregulated in MDA5 positive patients. Glycosaminoglycan binding and antioxidant activity were specifically dysregulated in TIF1-γ positive patients. Both patient subsets were compared with antibodies negative patients. We also found different immune pathway between three subsets. Such as innate and adaptive immune system play an important role in the pathogenesis of dermatomyositis. This study has identified unique expression pattern of transcripts in DM patients. This 'sub-grouping' approach could further be useful for clinical evaluation of DM patients and devising targeted therapeutics.

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A case of wong-type dermatomyositis with Anti-TIF1-γ antibody

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Anti-transcription intermediary factor 1 (TIF1)-γantibody have been identified in cases with cancer-associated DM. We report the first case of positive anti-TIF1-γantibody in Wong-type DM associated with parotid gland tumor and demonstrated the importance of detection of serum anti-TIF1-γantibody and screening tumor in Wong-type DM. The titer of the antibody was also closely correlated with the severity of cutaneous and the prognosis of the disease. Dynamic observation of serum anti-TIF1-γantibody levels would be helpful in predicting the course and facilitating better therapeutic targeting.

004

HRCT in accessing of interstitial lung disease in dermatomyositis with positive expression of anti-MDA5 autoantibody

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Objective. A newly described autoantibody to a 140-kDa nuclear protein, identified as melanoma-differentiation associated gene 5 (MDA5), were closely associated with life-threatening ILD in DM. Occult lung detection by HRCT (high-resolution computerized tomography) seems to be a good alternative to conventional screening of ILD. This study examined the antibody in the sera of patients with DM/CADM and described HRCT scores and findings in patients with positive anti-MDA5 antibody. Methods. We screened 79 patients with various CTDs, including 38 with DM/CADM (22 of DM, 16 of CADM). Anti-MDA5 antibody was detected by enzyme-linked immunosorbent assay (ELISA). Clinical and laboratory data were collected. Results. The level of anti-MDA5 antibody shown by the ELISA was significantly greater in the samples from patients with CADM than in those from patients with classic DM (194.9±377.5 vs 37.28±161.1, P=0.002). A/SIP was complicated more frequently in MDA5-positive patients than in those of MDA5-negative patients (66.9% vs 0, P=0.001). The HRCT scores of the MDA5 positive subset were increased compared with those MDA5-negative group (122.9±54.8 vs 70.0±59.8, P=0.041) and correlated with anti-MDA5 antibody level (r2=0.514, P=0.012). Conclusion. Anti-MDA5 antibody was found at an unusually high frequency in this group of Chinese patients. HRCT diagnosis should combine with the detection of anti-MDA5 antibody, which will help us to determine the pathologic type and prognosis of patients with DM/CADM.

005

Elucidating the mechanism(s) of silica nanoparticle induced immunomodulation in contact hypersensitivity

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Nanoparticle (NP) enabled consumer products and biomedical devices have become ubiquitous. Many examples exist of NP based products in the cosmetic, sunscreen, and textile industries. While currently used as an anti-caking agent in cosmetics and foods, silica NPs have been the focus of numerous transdermal drug delivery studies, which can lead to increased dermal exposure. Research on the lungs and gastrointestinal tract have highlighted a potential immunomodulatory capacity of NPs; however, additional research into the health effects of NPs on skin are warranted. To elucidate the effect of silica NPs on both healthy and inflamed skin, our lab topically exposed hairless C57BL/6 mice to a dinitrofluorobenzene (DNFB) allergen, with or without NP pretreatment, in the challenge phase of a contact hypersensitivity response. Previously we reported that topically applied 20 nm silica NPs decreased the DNFB induced ear swelling response, and this effect was characterized by decreased cytokine expression (IL-1β and MIP-2) and reduced cytotoxic T cell localization in skin 24 hours after DNFB challenge. To elucidate the mechanism of action of these NPs, we conducted a RNA sequencing study on whole skin samples. The transcriptome analysis revealed over 3400 differentially expressed genes in DNFB treated skin, compared to control skin. Pathway analysis reveals that many of the genes are involved in skin barrier repair, antioxidant response, and immune signaling. Interestingly, only 28 genes were differentially expressed in skin treated with both DNFB and silica NPs, compared to skin treated with only DNFB. Genes associated with fatty acid oxidation, activator protein-1 signaling, and antioxidant activity were all upregulated, compared to DNFB only samples. While more work is needed to identify whether changes in the transcriptome lead to functional changes in the skin, this data provides insight into potential mechanisms of silica NP induced skin immunomodulation.

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Topical application of caffeoyl prolyl histidine amide suppresses 2,4-dinitrochlorobenzene-induced atopic dermatitis-like symptoms in BALB/c mice

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The main components in atopic dermatitis (AD) pathogenesis are skin barrier abnormality, immunologic dysregulation, and pruritus. Considering the oxidative stress impacts on three main factors, we hypothesized antioxidant agents could be an effective treatment option in AD. To evaluate the effect of caffeoyl-prolyl-histidine amide (CA-L-Pro-L-His-NH2; CA-PH), a conjugated amide form of caffeic acid, 2,4-dinitrochlorobenzene (DNCB) was topically applied on the dorsal skin of BALB/c mice to induce AD-like symptoms and cutaneous lesions. CA-PH (0.5 mM and 5mM) or dexamethasone (25μg) was applied on the skin for two weeks to assess the relieving effects of DNCB-induced AD-like symptoms. CA-PH alleviated DNCB-induced AD-like symptoms quantified by dermatitis score, scratching behavior, and transepidermal water loss. Histopathological analysis revealed that CA-PH decreased DNCB-induced epidermal thickening, eosinophil and mast cell infiltration in dermis. We also found that CA-PH reduced serum IgE, and the mRNA levels of TSLP, interleukin (IL)-4, IL-25, IL-31, and IL-33 in the skin. This study showed that topical CA-PH could be a therapeutic option for AD.