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Analysis of the related factors that leading to the resistance of topical treatment for bullous pemphigoid patients

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Based on clinical and laboratory data, we analyzed the related factors leading to the resistance of topical treatment for BP patients. Totally 64 BP patients were enrolled in the study, and divided into two groups according to different methods of treatment. One of the groups contained 22 patients that showed effective to topical treatment. Another group contained 42 patients, who got more than 3 new blisters in the continuous 3 days during 4 weeks of the topical treatment, which showed resistant to topical treatment. The types of lesions, the BPDAI (Bullous Pemphigoid Disease Area Index score, Bullous Pemphigoid Diseases Area Index) , the concentration of albumin, eosinophil counts, the titer of anti-BP180 and anti-BP230 IgG, the concentration of total IgE, the titer of anti-BP180 and anti- BP230 IgE of the two groups were analyzed by GraphPad Prism5 software, and Mann Whitney inspection methods were used for statistical analysis. The results of analysis will be helped to select the proper treatments for different BP patients. The results showed that the main lesion type of the group that showed effective to topical treatment was simple blister (68 %), and the type of erythema with blister (63%) was the major type of the patients that resistant to topical treatment. The BPDAI, EOS counts, the concentration of total IgE, the titer of anti-BP180 IgG, anti-BP230 IgG, and anti-BP230 IgE were significantly higher in the group of patients that effective to topical treatment ($P < 0.05$). There's no difference of the concentration of albumin and the titer of anti-BP180 IgE between the two groups. So according to our study, in addition to BPDAI and anti-BP180 IgG titer, we can also select appropriate treatments for BP patients according to their lesion type, peripheral eosinophil counts, the concentration of total IgE, and the titer of anti-BP230 IgE.

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Study on detection of IgM and IgG of the anti-42000 protein from egg nucleus antibody in SLE patients's sera with Dot immunogold filtration assay

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Objective To develop a simple, fast and reliable assay for diagnosis of systemic lupus erythematosus (SLE) and evaluation of treatment effects. Methods Dot immunogold filtration assay (DIGFA) was used to detect the IgM and IgG in the anti-42000 protein from egg nucleus antibody in SLE patients's sera, and the geometric mean of reverse titer (GMRT) of IgM, IgG was detected in the sera of SLE patients before and after treatment. Results The positive rate of specific IgM and IgG in sera of 191 SLE patients was 94.24% and 92.15%($P>0.05$); No false positive and cross reaction were found in the sera from 100 normal individuals, 72 sera of dermatomyositis or polymyositis(DM/PM), 48 sera of progressed system scleroderma (PPS) and 78 sera of Mixed connective disease(MCTD). Among 174 SLE patients whose IgM and IgG were positive in their sera, before treatment their GMRT of IgM and IgG was 768.48±26.43 and 629.25±30.05 and after treatment it was 367.53±18.52 and 405.72±16.35 in 71 active SLE patients'sera ($P<0.01$). In 103 inactive SLE patients'sera, the GMRT of IgM and IgG was 421.34±23.12, 452.67±16.35 before treatment and it was 295.63±20.57, 358.73±21.37 after treatment($P<0.01$). Conclusion DIGFA can be an effective way to detect the IgM and IgG of the anti-42000 protein from egg nucleus antibodies in SLE patients' sera.

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Global proteomics and bioinformatic analysis of hyperthermia-induced differential protein expression in condyloma acuminata

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Hyperthermia has proved successful in treating cutaneous human papillomavirus infectious diseases such as plantar wart and condyloma acuminata (CA). Moreover, this treatment provides improved therapeutic efficacy in these conditions as compared with conventional therapies. In order to achieve a better understanding of the mechanisms of hyperthermia against HPV-infectious diseases, we applied a global proteomic investigation (iTRAQ) in CA tissues in response to *ex vivo* 44 °C hyperthermia (isothermal water bath). Compared to 37 °C counterparts, a total of 102 differentially expressed proteins (DEPs, with fold change greater than 1.2 or less than 0.833, p-value < 0.05) were identified in 44 °C groups (37 upregulated and 65 downregulated). K-means clustering and GO-BP enrichment analysis of the DEPs revealed that hyperthermia inhibited multiple processes related to energy and nucleic acid metabolism (GALT, H6PD, EXOSC4 and EXOSC6), as well as keratinocyte differentiation (KRT5, KRT27, KRT75, KRT76 and H2AFY2), whereas it stimulated processes involved with antigen presentation and anti-virus activity (OAS1, MX1, BANF1, CANX and AP1S1). Protein-protein interaction analysis of DEPs identified 68 interactions involving 49 different proteins (consisting of 2 major modules), whose GO-BP enrichment analysis results revealed similar pattern as those of k-means clustering of the overall proteomic changes. These results demonstrated that hyperthermia induces anti-viral activities whereas it inhibits metabolism and keratinocyte differentiation, which substantiate some of our speculations on the mechanisms of hyperthermia therapy and provide additional insights into some specific pathways through which local hyperthermia alleviates HPV infections. We believe these current results provide a foundation for future avenues of research into the detailed mechanisms involved with the efficacy of local hyperthermia and will guide us to improve the implementation of this promising clinical therapeutic method against cutaneous HPV infection.

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Comprehensive assessment of T cell receptor β repertoire in Stevens–Johnson syndrome/Toxic Epidermal Necrolysis patients using high-throughput sequencing

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Stevens–Johnson syndrome (SJS) /toxic epidermal necrolysis (TEN) are life-threatening severe cutaneous adverse drug reactions characterized by widespread epidermal necrosis. Recent studies have indicated that SJS/TEN is a specific immune reaction regulated by T cells. Certain drug serves as foreign antigens that are presented by major histocompatibility complex (MHC) and recognized by T cell receptors (TCRs), inducing adaptive immune responses. However, few studies have performed detailed characterization of TCR repertoire in SJS/TEN, and it remains unclear whether the particular types of TCRs expanded clonally are drug-specific, which would provide a potential underlying mechanism of SJS/TEN. In this study, using high-throughput sequencing, we comprehensively assessed the diversity, composition and molecular characteristics of the TCRβ repertoires in 17 SJS/TEN patients associated with three different causative drugs including methazolamide (MZ), carbamazepine (CBZ) and allopurinol (ALP). Systematic analysis of the TCRβ sequences revealed that SJS/TEN patients had more highly expanded clones and less TCR repertoire diversity, and the TCR repertoire diversity of these patients showed certain associations with the clinical severity of disease. Similar predominant clonotypes, shared-usage TRBV/TRBJ subtypes and combinations thereof were observed among different subjects with the same causative agent. Our observations provide enhanced understanding of the role of T lymphocytes in the pathogenesis of SJS/TEN and enumerate potential therapeutic targets.

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JAK inhibitors prevent and reverse vitiligo in mice, but do not eliminate established autoreactive T cells in the skin

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Vitiligo is an autoimmune disease in which autoreactive, cytotoxic CD8+ T cells destroy the pigment producing melanocytes, resulting in disfiguring, well-defined white patches on the skin. The IFN-gamma-induced chemokines CXCL9 and CXCL10, primarily produced by keratinocytes, are required to recruit autoreactive CD8+ T cells to the skin. Activation of the JAK/STAT pathway is required for efficient production of these chemokines and subsequent T cell recruitment. Targeting this critical pathway has been shown to work effectively for case studies. In this study, we aimed to reduce recruitment of the cytotoxic CD8+ T cells to the skin and prevent subsequent melanocyte death by inhibiting the JAK pathway with the small molecules inhibitors tofacitinib and ruxolitinib. We tested these JAK inhibitors in our mouse model of vitiligo as both prophylactic and therapeutic treatments. In prophylaxis experiments, these inhibitors lowered the clinical vitiligo scores, chemokine expression of CXCL10 within the epidermis and dermis, and reduced cytotoxic CD8+ T cell accumulation in skin compartments. In therapeutic treatments, mice with established vitiligo successfully repigmented their lesions. Surprisingly, repigmentation did not correspond to lower cytotoxic CD8+ T cells in the epidermal and dermal compartments. This finding echoes the use of secukinumab in psoriasis, where autoimmune signaling is disrupted but the resident memory T cells are not reduced and other recent case studies that also suggest that JAK inhibitors are not durable for vitiligo. These data further support the role of JAK inhibitors as a treatment in both the progression and maintenance of vitiligo, although they may not be a durable treatment.

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Single-cell transcriptomic level reconstruction of human psoriatic skin

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Psoriasis is an immune-mediated chronic inflammatory skin disease involving cell-to-cell communications within the lesional skin. Although psoriatic skins contain a highly increased number of cells with great heterogeneity, population diversity and single-cell level transcriptome expression within psoriatic plaques have been incompletely understood. Here we profile the transcriptomes of about 80,000 single cells from human psoriatic and normal skins to reconstruct a catalogue of lesional cell population. By aggregating whole individual cells, we identified 25 cellular clusters segregated by distinct patterns of gene expression. There were at least 4 different clusters of keratinocytes highly enriched in psoriatic skins expressing multiple keratin genes and *IL36G*. Although psoriatic fibroblasts would be classified into two main subsets by DPP4 expression as in normal skins, the majority of fibroblasts in psoriatic plaques expressed *CCL2* which would recruit CCR2+ inflammatory cells into the lesional dermis. Although both normal and psoriatic skins contained T cells with high level of *TIGIT*, psoriatic plaques harbored an additional population of *CD69*+ αβT cells expressing high level of multiple heat shock proteins, *REL*, *JUN*, and *FOS*, but negligible expression of checkpoint molecules. Population of *CCR7*+ migratory dendritic cells and *CD14*+*CD68*+ macrophages were also distinctly segregated between normal and psoriatic skins. Thus, our data provide a comprehensive catalogue of whole cell populations in the inflamed human skin which expanded our knowledge of cellular diversity in psoriasis.