**013**
Semaphrin4D drives CD8+ T cells skin trafficking in oral lichen planus via CXCL9 and CXCL10 upregulations in oral keratinocytes

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Chemokine mediate CD8+ T cell recruitment is an essential but not well-established aspect for the immune abnormality, chemokine modulation and cell migration, which are critical factors involved in OLP progression. We sought to elucidate the effect of Sema4D on human oral keratinocytes and its capacity to drive CD8+ T cell lesion trafficking through chemokine regulation. Sema4D and its receptors plexin-B1/phein-B2 and putative CD8+ T cell chemokines were examined in serum and lesions of OLP patients. The candidate chemokines were detected using quantitative real-time PCR and ELISA in oral keratinocytes treated with Sema4D. Involved mediators were analyzed using quantitative PCR, western blotting and ELISA. The migration of OLP CD8+ T cells mediated by Sema4D was tested using transwell assays. Up-regulation of Sema4D in OLP tissues and blood positively correlates with disease severity and activity. Sema4D induces CXCL9 and CXCL10 productions in human oral keratinocytes and OLP CD8+ T cells migrate toward Sema4D/E-selectin chemokines in vitro. Elevated levels of CXCL9 and CXCL10 in OLP positively correlate with Sema4D levels in lesions and serum. Sema4D through plexin-B1 over plexin-B2 via the Akt-NF-kB cascade induce CXCL9 and CXCL10 productions in oral keratinocytes. Sema4D binding to plexin-B1 by activating Akt-NF-kB cascade modulated CXCL9 and CXCL10 regulation in oral keratinocytes that elicit CD8+ T cells migration, which may be applied for OLP treatment.

**014**
A novel role of sensory nerves to establish contact hypersensitivity by promoting cutaneous dendritic cell functions via PACAP

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Circadian rhythms are closely associated with various biological processes in living systems. Several previous studies suggest that circadian rhythms can affect the mechanisms of the immune system and its related diseases. However, the effects of circadian rhythm disruption in the mechanisms of allergic skin inflammation has not yet been fully elucidated. The aim of this study was to assess the effects of circadian rhythm disruption on the contact hypersensitivity (CHS) by the perturbation of light environment, using a mouse model of CHS. Mice were kept under constant light (LL) or 12 h light:12 h darkness (LD) conditions and 5 weeks later, temperature was applied to abdominal skin for sensitization. Five days later, hapten was applied to ear skin for elicitation. The ear-swelling responses and infiltration of cells such as eosinophils, mast cells, CD4+ T-cells, CD8+ T-cells, or macrophages into infiltrated skin were evaluated. The ear-swelling responses and cell infiltration into infiltrated skin significantly were increased in LL mice in comparison with those in LD mice. In addition, the numbers of degranulated mast cells were greatly increased in LL mice compared with those in LD mice although the numbers of intact or total mast cells were not increased. Furthermore, the numbers of eosinophils were notably increased in infiltrated skin of LL mice compared with those in LD mice. These results suggest that disrupted circadian rhythms may exacerbate the CHS response via mast cell activation and eosinophil infiltration.

**015**
Effects of constant light exposure on contact hypersensitivity in mice

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Circadian rhythms are closely associated with various biological processes in living systems. The etiology of bullous pemphigoid (BP) is multifactorial in which the genetic aspect has been considered a critical susceptibility factor. Overexpression of Nrf2 regulates keratinocyte proliferation and is considered to be the hallmarks of psoriasis, the underlying mechanism accounting for overexpression of Nrf2 remains unclear. Nuclear factor (erythroid-derived 2) related factor 2 (Nrf2), a transcription factor known for its role in cytoprotection against oxidative stress, has recently been shown to regulate cell proliferation. Therefore, we investigated whether Nrf2 regulates keratinocyte proliferation via promoting expression of K6, K16 and K17 in psoriasis. In our study, we initially found that Nrf2 was activated in psoriatic epidermis, as assessed by subcellular localization, phosphorylation status, mRNA and protein expression. In this study, we observed that Nrf2 is a critical regulator of keratinocyte proliferation by activating the expression of keratin types K6, K16 and K17, which are physiologically related to psoriasis. Notably, we observed that Nrf2 activation in keratinocyte proliferation and pathogenesis of psoriasis. Blocking activation of Nrf2 might be applied in treatment of psoriasis in the future.

**016**
Hyperactivation of Nrf2 contributes to keratinocyte hyperplasia in psoriasis by promoting Keratin 6, 16 and 17 expressions

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Psoriasis is an inflammatory skin disease characterized by keratinocyte hyperproliferation of epidermis. Although hyperproliferation-associated keratins including K6, K16 and K17 are considered to be the hallmarks of psoriasis, the underlying mechanism accounting for overexpression of these keratins remains unclear. Nuclear factor (erythroid-derived 2) related factor 2 (Nrf2), a transcription factor known for its role in cytoprotection against oxidative stress, has recently been shown to regulate keratinocyte proliferation via promoting expression of K6, K16 and K17 in psoriasis. In our study, we initially found that Nrf2 was activated in psoriatic epidermis, as assessed by subcellular localization, phosphorylation status, mRNA and protein expression. In this study, we observed that Nrf2 is a critical regulator of keratinocyte proliferation by activating the expression of keratin types K6, K16 and K17, which are physiologically related to psoriasis. Notably, we observed that Nrf2 activation in keratinocyte proliferation and pathogenesis of psoriasis. Blocking activation of Nrf2 might be applied in treatment of psoriasis in the future.

**017**
The associations of HLA class I and II alleles in bullous pemphigoid

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The etiology of bullous pemphigoid (BP) is multifactorial in which the genetic aspect has been considered a critical susceptibility factor but not well-established factor for the development of BP. We aimed to determine the pathogenic role of HLA class I and II alleles in BP development among the Chinese population and their implication on the clinical features of BP patients. A total of 105 BP patients were enrolled for the genotype detection of HLA class I and II alleles. The results of HLA frequencies were compared between BP patients and unrelated healthy donors. The clinic connection of the HLA frequencies in BP patients was discussed as well. Among the HLA alleles described herein, the susceptibility alleles with highly prevalence was HLA-DRB1*10:01 and HLA-DPB1*04:01. HLA-DRB1*10:01 and HLA-DPB1*04:01 correlated with BP progression, which may be promising therapeutic target for BP treatment.

**018**
Intradermal administration of nor epinephrine (NE) biases topical immunization with dinitrofluorobenzene (DNFB) away from IFNγ, IL-22 and IL-4 responses and toward an IL-17A response

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We have previously reported preliminary results showing that exposure of primary dermal epidermal cells to NE biases the immune response towards an IL-17A response compared to IFNγ, IL-22 and IL-4. Here we show that when NE is administered intradermally, each with 1 μg of NE in phosphate buffered saline (PBS), mice were immunized 15 min later to DNFB by application of 100 μl of 1% DNFB in acetone:oil (4:1) at 1 site. Control mice were treated identically except that PBS without NE was injected at the sites of immunization. Additional groups of control mice were injected with NE or PBS followed by mock immunization with acetone:olive oil alone. Mice were euthanized 3 days after immunization, draining lymph nodes obtained and CD4+ T cells isolated by negative selection using magnetic antibody techniques. CD4+ T cells were expanded using anti-CD3 and anti-αCD28 antibodies. Sorted CD4+ T cells were harvested at 72 h and cytokine content assessed by ELISA. CD4+ T cells from mice immunized at NE-injected sites had a statistically significant increase in IL-17A release along with significant decreases in IL-4, IL-22, and IFNγ production. While the locus of action of NE in this type of vivo experiment is unknown, these results demonstrate that administration of NE into skin biases the induction phase of immunity to DNFB toward an IL-17A response. These results may suggest a role for the stress hormone NE in the regulation of immune responses and immune-mediated disorders in the skin. Hypothesizing the modulation of sympathetic nervous system, NE released in the skin may exacerbate skin disorders characterized by inappropriate Th17/IL-17A activation.