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

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PACAP plays an important role in initiating the CHS responses by inducing DC migration. Essential for cutaneous DC migration. These results indicate that sensory nerve-derived PACAP plays an important role in initiating the CHS responses by inducing DC migration.

Intradermal administration of nor epinephrine (NE) biases topical immunization with dinitrolfluorobenzene (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 microvascular endothelial cells to NE endows them with the ability to present ovalbumin (OVA) antigen-presentation to responsive T cells toward differentiation of Th17 helper cells. To assess NE effects on immune responses in vivo, naive BALB/c mice were injected at 2 sites on the back with OVA in complete Freund’s adjuvant or PBS in each 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-olive oil (4:1) at each site injected. 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-CD28 antibodies. Sorted CD4+ T cells were rested for 72 hrs before being added to cultures in the presence of CD8+ T cells, with CD4+ T cells cocultured as indicated. The results demonstrated 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. Hypothetically, under conditions of stress and activation of the sympathetic nervous system, NE released in the skin may exacerbate skin disorders characterized by inappropriate Th17/IL-17A activation.

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

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We aimed to determine the pathogenic role of HLA class I/II alleles in BP development considering a critical but not well-established factor for the development of BP. The clinic connection of the HLA frequencies in BP patients was discussed as well.

Psoriasis is an inflammatory skin disease characterized by keratinocyte hyperproliferation of the 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 cell proliferation. Therefore, we investigated whether Nrf2 regulates keratinocyte proliferation via promoting expression of keratins 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 of Nrf2. Overexpression of Nrf2 in human keratinocytes significantly increased cell proliferation but also increased expressions of K6, K16 and K17, vice versa. Furthermore, ChIP assays revealed that Nrf2 binds to the promoter of K6, K16 and K17 genes, further indicating a direct regulation of Nrf2 on K6, K16 and K17 genes. Additionally, upon stimulation of IL-17 and IL-22, Nrf2 was activated, translocated to the nucleus and induced expression of target keratins. Topical application of Nrf2 siRNA in mice with imiquimod-induced psoriasis alleviated the psoriasisform hyperplasia. In addition, the lesional level of K6, K16 and K17 were all reduced by Nrf2 blockade. Our findings indicated that in response to stimuli of inflammatory cytokines, Nrf2 activation in psoriatic lesions results in increased expression of hyperproliferation-associated keratins K6, K16 and K17, thus promoting keratinocyte proliferation and pathogenesis of psoriasis. Blocking activation of Nrf2 might be applied in treatment of psoriasis in the future.