014 A novel role of sensory nerves to establish contact hypersensitivity by promoting cutaneous dendritic cell functions via PACAP. Y. Fang,1 Y. Sun,2 L. Otsuka,1 Y. Nonomura1, K. Konishi2, M. Hayashi1 and Y. Yamamoto1 1 Department of Dermatology, Kyoto University, Kyoto, Japan and 2 Department of Dermatology, Kyoto University, Kyoto, Japan. Neuropeptides, such as PACAP, play an important role in initiating contact hypersensitivity (CHS) responses by inducing DC migration. These results indicate that sensory nerves contribute to the development of CHS via the promotion of DC migration.

017 The associations of HLA class I and II alleles in bullous pemphigoid. H. Fang, S. Shen, S. Zhang, C. Wang and J. Zhang 1 Xijing Hospital, The Fourth Military Medical University, Xi’an, China and 2 Xijing Hospital, Xi’an, China. Bullous pemphigoid (BP) is an autoimmune blistering disease and the HLA associations are of diagnostic and therapeutic significance. In this study, we investigated the associations of the HLA class I and II alleles in BP patients.

016 Hyperactivation of Nrf2 contributes to keratinocyte hyperplasia in psoriasis by promoting Keratin 6, 16 and 17 expressions. J. Yang, J. Fan and G. Wang 1 Xijing Hospital, The Fourth Military University, Xi’an, China. 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 keratin 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. Using lentiviral technology to increase Nrf2 expression, we also found increased expression of keratins K6, K16 and K17. Further, 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-23, Nrf2 was activated, translocated to the nucleus and induced expression of targeted 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 indicate 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 to treat psoriasis in the future.