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Allergy/angiogenesis

13-01/P

IL-31 IS ASSOCIATED WITH CLA+ SKIN-HOMING T CELLS IN PATIENTS WITH ATOPIC DERMATITIS

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Interleukin-31 (IL-31) is a newly discovered T cell cytokine which, when over-expressed in mice, results in pruritus and the development of skin dermatitis resembling human atopic dermatitis (AD). In this study, we investigated the expression of IL-31 and IL-31 receptor A (IL-31RA) in skin biopsies and peripheral blood cells from AD patients and normal individuals by IHC and RT-PCR. Our studies showed that although IL-31RA protein was expressed by keratinocytes and infiltrating macrophages in skin biopsies from both AD patients and normal skin samples, IL-31RA was expressed at higher levels on epidermal keratinocytes from the AD samples. Infiltrating cells, present at greater numbers in skin of AD patients compared to normal individuals, expressed IL-31 mRNA. Histomorphometric analysis of these cells indicated they were of the lymphocytic lineage, with the majority of cells staining positive for CLA and CD3. In addition, analysis of peripheral blood cells from AD patients and normal volunteers showed that IL-31 mRNA and protein expression was largely restricted to CD45RO+ (memory) CLA+ skin-homing T cells. Moreover, circulating CLA+ T cells from AD patients, but not patients with psoriasis, were capable of producing higher levels of IL-31 compared to CLA+ T cells from normal individuals. These results provide evidence that IL-31 expression is associated with AD and may contribute to the development of AD skin inflammation and pruritus.

13-02/P

DISTINCT PATTERNS OF LUNG CHEMOKINE RECEPTOR EXPRESSION DURING REMISSION AND EXACERBATION OF ALLERGIC ASTHMA IN MICE

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Acute allergic asthma in mice is induced by immunization and subsequent nebulization with ovalbumin (OVA) and is characterized by eosinophilic lung inflammation, mucus hypersecretion, elevated IgE, and airway hyperresponsiveness. Upon remission from acute disease, mice have persistent infiltrates containing memory Th2 cells, B cells, macrophages, and dendritic cells within lungs for over 800 days after disease initiation. Memory lung Th2 cells from recovered mice express a resting memory cell phenotype, respond *in vitro* to OVA by producing Th2 cytokines, and passively transfer disease to naïve mice. Moreover, *in vivo* OVA-aerosol exposure increases the expression of Th2 cytokine RNA and disease exacerbation. To elucidate a role for chemokine- chemokine receptor (CKR) interactions in the maintenance of long-lived lung Th2 memory in allergic asthma, we investigated CKR expression by RT-PCR, immunohistochemistry, and FACS in lungs from naïve, recovered, and secondary OVA aerosol challenged mice. CKR analysis revealed constitutive expression of CCR2, CCR5, CXCR4, CXCR5, and CX3CR1. Compared to naive mice, disease recovery was associated with up-regulation of CCR4, CCR6, CCR7, CCR8, CCR9, CXCR2, and CXCR3 and down-regulation of CCR1. Interestingly, the transition from disease remission to OVA-induced exacerbation 2 hours after aerosol challenge was characterized by a decrease in the expression of CCR4, CCR6, CCR7, CCR9, CXCR3, CX3CR1, and XCR1, suggesting receptor down-regulation and/or emigration of cells from the lungs. CCR1 and CCR3 were increased and no changes were observed for CCR8 and CXCR2. Our findings demonstrate that disease remission correlates with increased expression of several CKRs in the lungs, which is followed by their downmodulation during early disease exacerbation. Taken together, these data suggest that chemokine-CKR interactions may provide signals important for the survival and retention of persistent Th2 memory cells in lungs during remission of allergic asthma.

13-03/P

COMPARATIVE ANALYSIS OF INTERLEUKIN (IL)-6, IL-8, COX-2 IN HUMAN ASTROCYTOMAS. ASSOCIATIONS WITH VEGF EXPRESSION.

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Astrocytic tumours, particularly glioblastomas, are recognized to be highly vascular neoplasms with potent angiogenic activity. The aim of the present study was to examine the role of IL-6, IL-8, COX-2 in astrocytomas and to investigate any possible associations with VEGF expression. We determined the distribution of IL-6 and IL-8 using ELISPOT methodology in peripheral blood mononuclear cells of 17 glioblastoma patients, 5 diffuse astrocytoma patients (WHO grade II), and 1 oligoastrocytoma patient (WHO grade II), in parallel with 23 healthy controls. Immunohistochemical localisation of IL-6, IL-8, COX-2 and VEGF expression levels was also performed in formalin-fixed paraffin-embedded tissue sections of the same patients. We found that IL-6 was highly secreted in peripheral monocytes of astrocytomas compared to controls ($p < 0,001$) and it was further shown to be localized in the tumour cells and macrophages as well as in areas of ischemic necrosis within glioblastomas. IL-8 was secreted and expressed at high levels both in peripheral blood and tumour cells. Predominant IL-8 localization was on malignant cells or macrophages in perivascular areas and on pseudopalisading cells around necrosis. COX-2 was also detectable, in all cases, in the cytoplasm of neoplastic cells. There was a positive correlation between IL-6 and IL-8 ($p = 0,0182$) and between COX-2 and VEGF expression levels ($p = 0,0432$). IL-6 expression was positively associated with COX-2 and VEGF expression levels ($p = 0,04$, $p = 0,05$, respectively) as well as IL-8 expression with COX-2 and VEGF ($p = 0,0107$, $p = 0,0212$, respectively). IL-6 and VEGF expression levels were also found elevated in glioblastomas compared to low grade astrocytomas ($p = 0,02$, $p = 0,0221$, respectively). A positive correlation between IL-6 expression and secretion levels ($p = 0,01$) v was also identified. These results implicate IL-6, IL-8 and COX-2 in the angiogenesis of diffuse astrocytomas. Therefore, we suggest that IL-8 is critical to glial tumour neovascularity and progression, whereas IL-6 provides an additional growth advantage.