and p40. The IL-12 p35 mRNA was expressed in PBMCs from AD patients, but not in PBMCs from normal controls (Fig. 1B). However, no p40 mRNA expression could be detected using three different sets of published primers.[3,9,18]

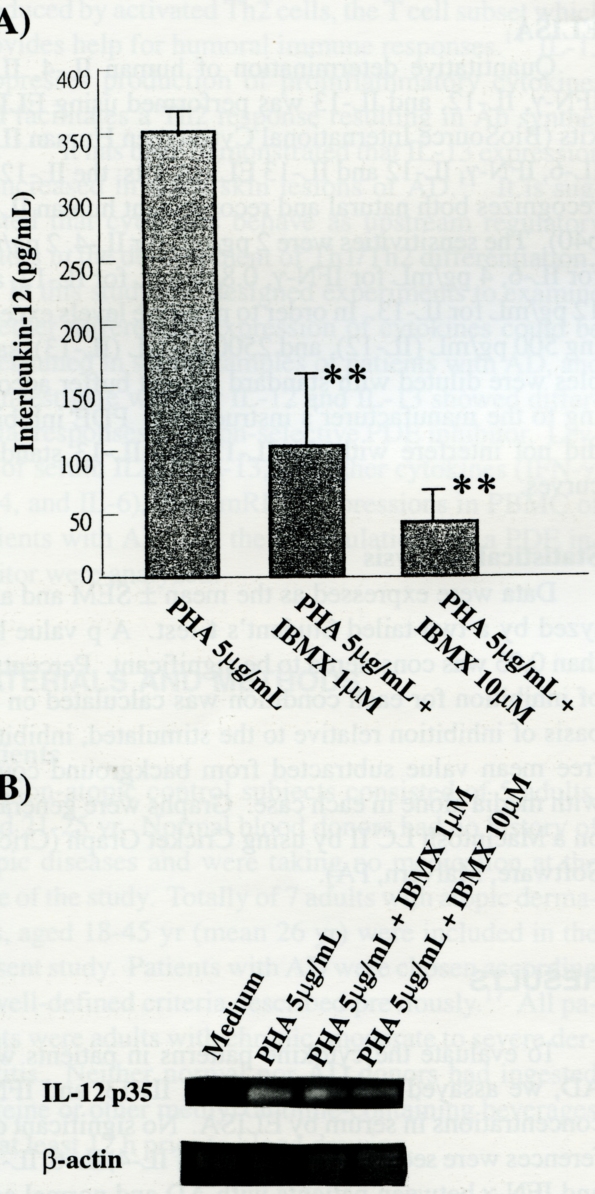

Fig. 2. IBMX inhibited IL-12 secretion and IL-12 p35 mRNA expression in PBMCs from atopic dermatitis patients. (A) Secretion of IL-12 was inhibited by IBMX in PBMCs from AD (n = 7). Data were expressed as the mean ± SEM. (PHA stimulation only vs. IBMX treatment: **p < 0.01) (B) Detection of IL-12 p35, and β-actin mRNA expression using RT-PCR. Lane 1, medium; Lane 2, PHA 5 μg/mL; Lane 3, PHA 5 μg/mL + IBMX 1 μM; Lane 4, PHA 5 μg/mL + IBMX 10 μM.

Previous reports have shown that the PDE inhibitor produced nearly identical concentration-dependent inhibition for prostaglandin E2, IL-4, and interleukin 10 (IL-10) in AD mononuclear leukocyte cultures.[18,19] Since IBMX is a common PDE inhibitor,[7] the effect of IBMX on IL-12 levels was assessed. The inhibitory effect of IBMX on IL-12 production in PBMCs cultures stimulated by PHA (5 μg/mL) is shown in Fig. 2A. Without inhibiting the proliferation of PBMCs (data not shown), IBMX inhibited IL-12 production in a concentration-dependent manner ($p < 0.01$) (Fig. 2A.). To investigate whether IBMX would decrease IL-12 p35 mRNA expression, a similar study on PBMCs treated with IBMX (concentrations ranging from 1 to 10 μM) was performed. IL-12 p35 mRNA expression was inhibited by increased IBMX concentrations (Fig. 2B).

DISCUSSION

Th1/Th2 clones were differentiated on the basis of their cytokine production profiles: Th1 cells produce IL-2 and IFN-γ, and Th2 cells primarily secrete IL-4 and IL-5.[20] Previous studies have demonstrated a predominant Th2 activation in atopic diseases.[22] IL-12 preferentially induced the development of Th1 cells. However, in the present study, elevated serum IL-12 secretion was found in chronic, moderate to severe AD patients. Serum IL-4 was increased in only one AD patient. Hamid et al. demonstrated that IL-12 mRNA expression was increased in skin lesions of chronic atopic dermatitis.[11] All the patients studied here were chronic AD patients. To the best of our knowledge, this is the first finding of increased serum IL-12 production in atopic dermatitis. The finding may support the role of IL-12-producing cells in modulating chronic inflammation.

It has been shown that IL-12 preferentially induces the development of Th1 cells[4] and thereby increases the synthesis of IFN-γ,[6] a potent inhibitor of IL-4-induced responses. With increased serum IL-12 levels, no IFN-γ was detected in the AD patients. Lester et al. demonstrated that PBMCs from patients with AD synthesized significantly lower amounts of IFN-γ in response to IL-12 than to PBMC from normal donors, and their differential response to IL-12 was not due to decreased expression of the IL-12 receptor on T cells from AD patients.[12] Although activated T cells express both low