and high affinity receptors of IL-12,[21] it is likely that PBMCs of AD patients express normal numbers of low-affinity IL-12 receptors but are deficient in functional high-affinity IL-12 receptors. Oversecretion of IL-12 may just be feedback of low IFN-γ in AD patients. Our results suggest that non-detectable IFN-γ production is an intrinsic defect of PBMCs with AD itself. Further studies are needed.

IL-12 consists of a smaller p35 subunit and a larger p40 subunit,[2,3] and a p70 heterodimer is the only functional molecule. Although spontaneously increased secretion of IL-12 was demonstrated by ELISA, only p35 mRNA but not p40 mRNA was detected by RT-PCR. The kit can detect p70 and p40 based on the manufacturer's information. Improper PCR primers, inadequate PCR conditions, and extremely unstable mRNA may result in a nondetectable p40 message. Three published primer sets and amplification conditions were tested; it is very unlikely that the nondetectable IL-12 p40 message was due to technical problems. A similar finding was observed by Fujimura et al.[22] They found that PBMCs from AD patients express p35 mRNA upon in vitro stimulation with live vaccinia zoster virus, but no p40 mRNA without stimulation. This is an interesting finding in AD patients and needs to be further substantiated.

Hanifin et al. has demonstrated that peripheral blood mononuclear leukocytes from AD patients showed elevated cAMP-specific PDE activity.[1] PDE inhibitors reduced hyper-IgE synthesis in AD[19] and reduced prostaglandin E_2, IL-4, and IL-10 production in atopic mononuclear leukocyte cultures.[23] The non-selective PDE inhibitors such as theophyllin have been used for decades in the treatment of allergic disease[24] and the use of the topical type 4 PDE inhibitor, CP8-633, causes clinical improvement.[25] The non-selective PDE inhibitor, IBMX inhibits IL-12 production and secretion. IL-12 was shown to induce the synthesis of IFN-γ.[12] This result thus has implications for in future drug design based on the observed effect of PDE inhibitors on allergic disease.

IL-13 is produced mainly by activated T cells of the Th2 subset, and it shares a number of biological activities with IL-4.[15] In this study, neither ELISA nor RT-PCR could detect IL-13 expression in chronic, moderate to severe AD patients. A recent publication by Takamatsu et al. demonstrated IL-13 production from patients with AD.[26] They analyzed 52 patients; not all 52 cases had increased IL-13 production, with 8 moderate to severe cases below the detection level. Hamid et al. suggested that IL-13 may play a role in the pathogeneis of acute AD. IL-13 production may not be a common phenomenon in all AD patients. The discrepancy in findings may be due to differences in selecting patients.

In summary, enhanced expression and secretion of IL-12 in chronic AD patients were demonstrated, and the IL-12 production was inhibited by PDE inhibitor, IBMX. IL-12 had the ability to suppress IgE production in vitro by both IFN-γ-dependent and IFN-γ-independent mechanisms.[11] These data suggest that IL-12 may play an important role in the pathogenesis of AD, and the mechanism of PDE inhibitor in helping AD patients is partly through inhibiting Th2-type cytokine[18] and IL-12 at the same time. These findings thus provide a fresh avenue to design new therapeutics for this kind of skin disease.

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