Chapter V

Discussion

IL-18 (interferon-γ-inducing factor), a new potent proinflammatory cytokine, involves in both specific and non-specific immune effector mechanisms. In the specific effector arm, IL-18 acts as a co-stimulator of IL-12 dependent and IL-12-independent IFN-γ production by CD4+ T cells and NK cells, respectively.(36) In the other arm, it also directly induces other proinflammatory cytokines i.e., TNF-α and IL-1β production by PBMCs and enhanced NK cytolytic activity.(42-44) In the present study, constitutive expression of IL-18 gene was observed in PBMCs either from HIV seronegative controls or in those from HIV-infected individuals regardless of their CD4 cell counts. This is the first finding to show that IL-18 gene expression was not dysregulated in PBMCs despite in advanced HIV-infected patients. This finding may correlate with the broad properties of this cytokine, which has been described above. The redundant sources of IL-18 including monocytes/macrophages, and cells other than those of immune system may prevent its dysfunction from HIV infection. The spontaneous expression of IL-18 in PBMCs from healthy HIV seronegative individuals may indicate that although in the physiological state, IL-18 is essential for the immune system. It may play a role in maintaining preferential Th1 profile in normal setting. The clear-cut physiological role of IL-18 production in resting PBMCs, however, awaits further investigation.

RANTES and MIP-1α are potent suppressive factors for CCR-5 tropic HIV (R-5 virus) entry of many T cells, monocytic cell lines and mononuclear phagocytes in the blood and lung (88). PHA-induced RANTES and MIP-1α productions in PBMCs of HIV-infected persons, long-term nonprogressors (LNTP) in particular, were significantly higher than those of HIV seronegative individuals (20,21). In advanced HIV-infected individuals treated with protease inhibitor containing regimen; RANTES, MIP-1α and MIP-1β were found to be significantly increased (measured by EIA), in the contrast with the marked reduction of plasma HIV-RNA (89). In the present study, spontaneous expressions of RANTES and MIP-1α in PBMCs were observed in all of the subjects regardless of their HIV infection status. The qualitative RT-PCR used in this study, however, could not provide a comparative analysis in a quantitative manner. For further study more precise quantitative comparison, a

proper quantitative RT-PCR such as the assay that includes an internal control should be used in the further study

It should also be noted that the MIP-1α primers kindly provide by the Cellular Technology Institute, Otsuka Pharmaceutical, Japan ; was indeed a cloning primer which containing *Bam*HI site. This may affect by enhancing the efficiency of PCR and generate saturated product. For the further use, the PCR conditions need to be optimized and it is better to obtain a new primer set without the cloning site.