Abstract of Presentation

Note: This paper should be typed in "Times New Roman" of 12pt.

Presentation Title(Should be no more than 20 words):

Pharmaco- and immunogenetics upon HIV-1 infection

Abstract :

In this workshop, I will talk about pharmaco- and immunogenomics upon HIV-1 infection. Human cytochrome P450 2B6 (CYP2B6) metabolizes a number of drugs including an HIV-1 drug, efavirenz (EFV). EFV shows potent anti-HIV-1 activity and is stated as a key drug of the first line regimens in the HIV-1 treatment guideline. However, some patients treated with EFV develop central nervous system symptoms which are more frequent in patients with high plasma concentration of EFV. Recently, we reported that homozygote of *CYP2B6*6* is associated with the high EFV concentration and we can reduce the dose of EFV in those patients that allows side effects milder with maintaining viral suppression. Frequency of *CYP2B6*6/*6* in Japanese is only 4%, whereas that in Zambian is around 18%. Furthermore, we found that other alleles, *18 and *26, are also associated with the high EFV concentrations and, in overall, nearly 30% of Zambians had the high EFV concentrations. EFV must be widely used in African countries in near future. Therefore, clinical relevance of these SNPs is to be elucidated.

The natural course of HIV-1 infection has been well described; primary HIV-1 infection is followed by a clinical latency, usually lasting around 10 years, which precedes the eventual collapse of the immune system. However, there is a common feeling among clinicians at present that the natural disease progression of recently infected patients is faster than in previous years. Some HLA type is protective against disease progression such as HLA-B57 because HLA-restricted cytotoxic T lymphocytes (CTLs) play an important role on viral control. On the other hand, virus can easily escape from CTLs. In some prevalent HLA types, escape virus can transmit and accumulate in the population. In this situation, some HLA types are no more protective. In recent years, most HIV-1 infection in Japanese is transmitted from Japanese patients. It can be postulated that current HIV-1 in Japan has adapted to the Japanese population, indicating acquisition and accumulation of escape virus from immune pressure of the otherwise protective HLA in Japanese population. The clinical relevance of the prevalence of immune escape virus in Japanese is a potentially serious matter in terms of the natural course of HIV-1 infection.