(용역-5)

Long-term intake of Korean red ginseng destroys HIV-1 *nef* gene: a possibility as therapeutic vaccine 2004. 5. 11.

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Introduction of highly active antireroviral drug therapy (HAART) has given much hope to human immunodeficiency virus-1 (HIV-1) infected patients (1,2). However, this therapy alone cannot eradicate the virus in human body because of long-lasting provirus in the reservoirs (3-5). Although IL-2 has been tried into AIDS therapy as combination therapy with HAART, it has many limitations to continuous application. Thus, a new modality is required for more effective AIDS therapy.

We have obtained various beneficial effects by KRG-intake since 1991 (6-9). Among the 90 patients who were previously determined for HLA-class I, we seleted all living patients who have been checked for CD4 T cell over 10 years and have not been treated with antiretroviral therapy. They were 31 (The number corresponds to about 10% out of all 311 HIV-1 patients diagnosed up to October 1993 in Korea). We divided them into 2 groups according to the amount of KRG-intake we have supplied since 1991; group A with consistent and significant KRG-intake and group B with a little or no KRG-intake. Groups A and B were treated with KRG (7,971±3,853g) for 135±14 months and with KRG (992±1069g) for 125±19 months between the first and last CD4 T cell counting. Although CD4 T cell count significantly decreased at 2 groups ($P<0.001$), the degree of decrease at group A (155/ul; annual decrease of 14/ul) was greatly less than that (456/ul; annual decrease of 44/ul) at group B. Our data in group B underestiamte the rate of decrease in CD4 T cell in our cohort because the patients who had rapidly progressed to AIDS and died within 10 years after diagnosis were not included in the present study. On the other hand, HIV-1 RNA copy was lower at group A than B ($P<0.01$) and the number of patients with protective HLA alleles was higher than at group B ($P< 0.05$).

HIV-1 *nef* is essential gene for the progression to AIDS. Gross deletion in the nef gene (>more than 40 bp) has been rarely reported in LTNPs. Rhodes et al reported that the patients who revelaed gross deletion was 3 out of 70 LTNPs (4.3%)(10). Thus, to investigate whether there is an association between slow progression by KRG-intake and gross deletion in the nef, we have determined *nef* gene sequences (about 630 bp)

from 138 patients. In some patients, it has been determined over 10 years. In the present study, we present data from 115 excluding 23 hemophiliacs originating from a few common sources. The 115 patients are divided into 77 subtype B HIV-1 and 38 non-subtype B HIV-1 and also divided into 2 groups according to KRG-intake or not. Gross deletion was detected 35.1% (27/77) in patients with subtype B, whereas it was detected 15.8% (6/38) in patients with non-subtype B.

In subtype B, there was a strong causal relationship between KRG-intake and gross deletion (2/24 versus 25/53; $P<0.001$). Nature of gross deletion in the present study greatly differs from previous studies; in particular, the deletion extended beyond nef gene in 12 out of the 27 patients. Fourteen patients showed wild type nef only at baseline and significant period, and then revealed deleted one. First detection of gross deletion was 22 months (median)(range; 4-128) after KRG-intake. Except 2 sequences with Δ of 41 bp and 94 bp, size of deletion was larger than 100 bp (11). Regarding progression rate to AIDS, gross deletion was detected in 10 (76.9%) out of 13 LTNPs and 4 (30.8%) out of 13 NG ($P<0.05$), indicating a strong association between slow progression and gross deletion. In contrast, there was no such causal relationship in patients with non-subtype B. These data show that long-term intake of KRG destroys HIV-1 virus in vivo and therby significantly delays progression to AIDS. This finding suggests that KRG-intake have played as therapeutic vaccine.

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