A Population-based Matched-cohort Study on Insertion/Deletion Polymorphism of the APOBEC3B gene and Risk of HIV-1

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Background: The human APOBEC (A3) family proteins (A3A-H) potently inhibit replication of HIV-1. In human populations, a high-frequency distribution of the A3B deletion genotype is observed. Previously, several groups have reported controversial observations on the effect of A3B gene deletion on HIV-1 acquisition and disease progression. Here, in order to verify the effects of A3B on HIV-1 infection in vivo, we investigated the insertion (I)/deletion (D) polymorphism frequencies of the A3B gene in a matched cohort in Japan.

Methods: The A3B genotype was analyzed by PCR with genomic DNA from blood or buccal membrane. The effect of A3B gene deletion on disease progression was evaluated by comparing acquisition of Syphilis, HBV and HCV, as well as CD4+ T cell counts and viral load before starting cART among three genotype groups; deletion-homozygous (D/D), hemizygous (D/I), and no deletion (I/I) genotypes. Susceptibility to HIV-1 infection was assessed based on the frequencies of three genotypes between the infected and uninfected cohorts. HIV-1 replication kinetics and the infectivity were assayed in vitro by using healthy donor CD4+ T cells. Fischer exact and Mann-Whitney U tests were used for statistics.

Results: 228 HIV-1-infected patients of Japanese men who have sex with men (MSM) and 207 uninfected Japanese MSM were enrolled. Our A3B genotyping analysis showed no significant difference in the ratio of A3B genotype between the infected (D/D 8.3%, D/I 44.7%, and I/I 46.9%) and the uninfected (D/D 8.7%, D/I 39.6%, and I/I 51.7%) cohorts (p=.55). In addition, the parameters of disease progression resulted in quite similar frequencies among the three genotype groups. These results suggest no significant effect of A3B gene polymorphism on the HIV-1 transmission or the disease progression. Furthermore, the in vitro kinetics of HIV-1 replication and the infectivities of the virus in CD4+ T cells were comparable between D/D and I/I (p=.31 and p=.86, respectively).

Conclusion: Our analysis of a population-based matched cohort showed that loss of A3B gene is not associated with the risk of HIV-1 susceptibility and disease progression. The results suggest in vivo, A3B could play an unknown role, but not in eliminating HIV-1.