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Assessment of HIV-1 *Tat* gene sequence changes and its relation to HIV-1 stages in patients with HIV-1 in Iran

Samaneh Moallemi
Iranian Research Center for HIV/AIDS - Tehran University of Medical Sciences, Iran

Background: Central to HIV infection is the transactivator protein Tat, which plays a critical role during the HIV infectious cycle. Since blocking Tat protein is likely to prevent HIV infection, delineation of Tat is critical to assessing its viability as a therapeutic target. The aim of this study was to determine the association between changes in HIV-1 *Tat* gene sequence and three CDC defined stages of the disease.

Methods: Blood samples were collected from 87 HIV-1 patients in three stages of the disease; Tat gene mutations and subtyping were then determined by sequencing tat exon 1 region. SPSS software with Kruskal-Wallis and Tamhane tests were then used to assess the correlation between Tat sequence variation and HIV-1 disease stages.

Results & Discussion: Phylogenetic analysis showed that the most common subtype was CRF35-AD (79.41%); CRF-BFs, A and B were the other determined subtypes. Amino acid sequences of exon 1 of Tat protein in CRF35-AD showed two well-conserved regions (domain 3 and 4) while the fifth domain had the greatest genetic variability. SPSS statistical analysis revealed significant differences between the Tat sequence variation and two stages of HIV-1 disease (A, C). Studying Tat domains, the same conclusion was obtained for the 1st domain of Tat, however this relation was not found between HIV stages and other domains. This can be because the N-terminus of Tat is the major area of the epitope for the cytotoxic-T-lymphocytes (CTLs) that changes in these residues can change the function of Tat and it may modify the disease progress.

Conclusion: Regarding HIV drug resistance and side effects of highly active antiretroviral therapy (HAART) and the functional role of Tat protein in virus activity, further studies on molecular mechanisms of this protein may ultimately improve the quality of life of HIV-1 patients through the discovery of new pharmacological targets.

moallemi.samaneh@gmail.com