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HIV-1 Tat up-regulates Secretory Leukocyte Protease Inhibitor (SLPI) expression in African Green Monkey (AGM) cells and leads to the suppression of HIV-LTR promoter

Selcuk Ozdemir, Burcu Şengez and Alper Arslanoglu
Izmir Institute of Technology, Turkey

Statement of the Problem: Human immunodeficiency virus type 1 (HIV-1) leads to AIDS in humans by reducing CD4(+) T lymphocytes which are crucial for proper adaptive cellular and humoral immune responses. Old World Monkeys (OWM) on the other hand is resistant to HIV-1 infection. Although these monkeys can be successfully infected by monkey adapted HIV-1 strains, they eventually clear the infection and virus numbers drop to undetectable levels unless the animals are immune-compromised by CD8 cell depletion during and after experimental infections. These results indicate the possibility of the presence of yet unidentified factor(s) that restrict HIV-1 in OWM cells after integration of the viral genome into the host cell. The purpose of this study was to investigate whether any anti-HIV factors were expressed in AGM cells in the presence of HIV-1 Tat protein. Tat is among the first viral proteins produced in infected cells and is known to affect the expression of many human host genes as well as HIV's own gene expression.

Methodology & Theoretical Orientation: SLPI was identified by 2D-PAGE and mass spectrometry using MALDI TOF. Over expression of SLPI gene was investigated by qRT-PCR on mRNA, and by western blot on protein level, using anti SLPI antibodies. SLPI's effect on NF-kB and HIV-LTR promoter was investigated through the luciferase reporter gene expression.

Findings: We identified that SLPI expression was highly upregulated in presence of HIV-1 Tat in AGM but not in human cells. Furthermore, we showed that SLPI decreased both NF-kB and HIV-LTR promoter driven luciferase reporter gene expressions.

Conclusion & Significance: SLPI is a potential HIV-1 restricting protein. It leads to reduced viral replication in infected cells and should be further investigated. In such case, SLPI can open new avenues in the treatment of HIV-1 infection.

Recent Publications

1. Law K M, Satija N, Esposito A M and Chen B K (2016) Cell-to-cell spread of HIV and viral pathogenesis. *Adv Virus Res* 95:43-85.
2. Saito A and Akari H (2013) Macaque-tropic human immunodeficiency virus type 1: breaking out of the host restriction factors. *Front. Microbiol.* 4:187.
3. Theodora H, Gregory Q, Del P, Brandon F K, Jacob D E, Matthew W M, Julia B, Alice R, Anthony R, Fabian SC, Mac T, Jeremy S, Michael P J, Vineet N K, Jeffrey D L and Paul D B (2014) HIV-1-induced AIDS in monkeys. *Science* 344:1401-1405.
4. Musinova Y R, Sheval E V, Dib C, Germini D and Vassetzky Y S (2016) Functional roles of HIV-1 Tat protein in the nucleus. *Cell. Mol. Life Sci* 73:589-601.
5. Yoshikazu M, Takashi I, Yusuke K, Naoyuki M, Hidero O and Kazuo K (2015) Secretory Leukocyte protease inhibitor inhibits expression of polymeric immunoglobulin receptor via the NF-B signaling pathway. *Molecular Immunology* 67:568-574

Biography

Selcuk Ozdemir has expertise in mammalian gene expression analysis, environmental toxicology and animal genetics. He currently works as Assistant Professor at Ataturk University, Faculty of Veterinary Medicine.

alperarlanoglu@iyte.edu.tr