Fatah Kashanchi, J Antivir Antiretrovir 2011, 3:4
doi: http://dx.doi.org/10.4172/1948-5964.S1.4

International Conference and Exhibition on
VIROLOGY
5-7 September 2011 Baltimore, USA

Role of chromatin and microRNA in regulating HIV-1 transcription

Fatah Kashanchi
George Mason University, USA

Human immunodeficiency virus type 1 (HIV-1) Tat transactivation is an essential step in the viral life cycle. Over the past several years, it has become widely accepted that Tat exerts its transcriptional effect by binding the transactivation-responsive region (TAR) as well as P-TEFb and enhancing transcriptional elongation. The SWI/SNF complex remodels nucleosomes, allowing RNA Polymerase II access to the HIV-1 proviral DNA. It has not been determined which SWI/SNF complex (BAF or PBAF) remodels nucleosomes at the transcription start site. We show that PBAF is required for chromatin remodeling at the nuc-1 start site and transcriptional elongation. Interestingly, the BAF complex was observed on the LTR whereas PBAF was present on both LTR and Env regions. We found that Tat activated transcription facilitates removal of histones H2A and H2B at the LTR, and that the FACT complex may be responsible for their removal. The SWI/SNF complexes also play a major role in generation of Viral microRNA (i.e., TAR RNA) in HIV infected cells. We have recently developed a third generation derivative called CR8#13, which specifically inhibits cdk9 complex. When drugs, specifically Flavopiridol and CR8#13 are added, the transcriptional inhibition of the LTR was less potent in cells that lacked Dicer (monocytes). We find that the addition of CR8#13 could possibly increase levels of TAR microRNA in HIV-1 LTR containing cells. MicroRNA recruitment results in chromatin alteration, changes in Pol II phosphorylation and viral transcription inhibition. Therefore, our results indicate that viral microRNA, specifically the TAR microRNA produced from the HIV-1 LTR is responsible for maintaining latent infections by manipulating host cell mechanisms to limit transcription from the viral LTR promoter.

Biography

Dr. Kashanchi received his PH.D. from the University of Kansas in Microbiology and continued with his postdoctoral research in virology at NIH (National Cancer Institute) in Washington D.C. for more than 7 years. He is currently the director of research at George Mason University's National Center for Biodefense and Infectious Diseases. Dr. Kashanchi has published more than 127 papers in reputable journals and serves on a number of national advisory and review committees, including a total of nine NIH and National Science Foundation (NSF) study sections.