Lawrence Kleiman, Virol-mycol 2015, 4:2
http://dx.doi.org/10.4172/2161-0517.S1.002

OMICS International
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International Conference on
Retroviruses & Novel Drugs

June 08-09, 2015 Chicago, USA

Viral and host factors regulating the annealing of primer tRNA^{Lys3} to HIV-1 genomic RNA

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During HIV-1 infection, the conversion of the HIV-1 RNA genome into a double-stranded DNA that can be integrated into the host cell's genome is accomplished by reverse transcription. The initiation of this reverse transcription requires a specific cellular tRNA^{Lys3} to act as a primer. This tRNA is annealed during assembly of new HIV-1, i.e., the infecting virus already contains annealed tRNA^{Lys3}. The 3′ 18nts of tRNA^{Lys3} anneal to a complementary 18nt sequences in the viral RNA termed the primer binding site (PBS), and in this presentation, we will discuss the cellular and viral factors that promote the ability of the tRNA^{Lys3} to locate the 18nt sequence within the >9 KB comprising the HIV-1 viral RNA genome. This is associated with the formation of an early HIV-1 assembly intermediate at the site of the Gag/GagPol translation, whose components include Gag, GagPol, lysyl-tRNA synthetase (LysRS), and tRNA^{Lys3}. This intermediate contains an increased concentration of tRNA^{Lys3}due to a specific interaction between viral Gag and LysRS, and is able to bind through LysRS to a viral RNA structure near the PBS that resembles tRNA^{Lys3}. This initial cytoplasmic annealing of tRNA^{Lys3} to viral RNA is part of a multi-staged annealing process, and not only functions in promoting reverse transcription, but also facilitates a conformation change in the 5′-untranslated region of viral RNA that promotes viral RNA dimerization.

Biography

Lawrence Kleiman completed his Ph D at Johns Hopkins University, and after Postdoctoral studies at the Beatson Cancer Institute in Glasgow, Scotland, he has spent the remaining of his career at the Lady Davis Institute for Medical Research, Jewish General Hospital, in Montreal, Quebec, where he is also a Professor in the Department of Medicine at McGill University. He has published over 140 papers, and has worked for the last 20 years studying HIV-1 replication at the McGill AIDS Centre.

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