Selection of non-synonymous amino acid substitution by HIV during early infection: Variants identified by high-throughput sequencing

Ashokkumar Manickam[1,2], **Haleh Ganjian[2]**, Sathyamurthi Pattabiraman[1], Srikanth P Tripathy[1], Ujjwal Neogi[2,3], Luke Elizabeth Hanna[1]*.

Affiliations

1Department of HIV/AIDS, National Institute for Research in Tuberculosis, Chennai, India.

2Division of Clinical Microbiology, Department of Laboratory Medicine, Karolinska Institute, Stockholm, Sweden.

3Department of Molecular Microbiology and Immunology, University of Missouri, Columbia, MO 65211, USA.

Abstract

Background

Understanding the evolutionary dynamics of the viruses within individual at very near the moment of transmission is essential for designing effective vaccine (both, therapeutic and preventive) for the prolonged success against HIV-1 infection. It is important to examine minor genetic variations that occur within the population to characterize the host adaptation of viral quasispecies and their evolution towards drug resistance and immune evasion. It is often difficult to distinguish minor mutations that exist in the viral population through Sanger sequencing. On the other hand, high-throughput sequencing (HTS) technology provides enough throughput data and sensitivity to detect very rare viral mutations.

Methods

We employed Next-generation Sequencing (NGS) technology to analyse the evolutionary rates of samples at single time point acquisition from drug naïve recent and later stage infection. Nonsynonymous (dN) and synonymous (dS) rates along each and every gene were estimated.

Results

We found reasonable differences in the evolutionary rates of the different stages of infection. The substitution rates were also different between individuals infected recently through MTCT, with higher substitution rates in both *env* and *nef*. When compared to later infection, the number of SNPs in *env* was found lower in recent infection, but the conversion of non-synonymous mutations reversed to be higher in recent infection. Despite non-significant number of samples between recent and chronic stages of infection, we did find useful information about viral evolution on transmission-associated bottlenecks.

Conclusion

The effect of intra-individual HIV-1 evolution at the population level is highly contemporary, and the massive number of non-synonymous substitution rate in recent HIV-1 infection, particularly in the *env,* might have resulted from a pattern of convergent evolution leading to positive selection for survival fitness and disease progression.

Key words: Human Immunodeficiency virus type I, Next Generation Sequencing, Single nucleotide polymorphism, Synonymous and non-synonymous substitution and Viral evolution.