Abstract

Over 33 million people across the world are currently infected with the human immunodeficiency virus (HIV) while 30 million lost their lives since the initial cases of HIV were noted way back in 1980s. Noteworthy is the fact that unparalleled progress has been made since then to understand the virus and evolve means and ways to address the deadly disease caused by it. But equally important is the fact that the amazing adaptability of the virus that challenges almost all the tools of medical science developed against it. This underlines the need for a continued effort to keep learning about the strength and weakness of this pathogen and also develop methods that can assist clinicians in taking more informed therapeutic decisions towards their HIV infected patients. This thesis is a compilation of my research work addressing some of the pertinent issues related to HIV in India and elsewhere.

Through a well designed research targeted to scan region specific genome signatures I demonstrated nucleotide signatures unique to Indian isolates of HIV-1. The use of partial \textit{p24} gene sequence where such motifs were detected can function as tool for subtyping as well as phylogenetic grouping with special reference to its geographical location.

This thesis also reports a HIV-1 viral load assay which is robust, reliable, economical and effective in resource limited settings like India. PCR probes specially designed from HIV-1 Subtype C-specific nucleotide sequences originating from India were shown to impart specificity towards such isolates and demonstrated superior results when compared to two similar commercial assays widely used in India.

Through an extensive study spanning across 206 HIV-1 \textit{RT} gene sequences generated in this program, an effective and economical HIV-1 drug resistance genotyping method was developed. The evaluation of this assay on the clinical panel demonstrated its potential for monitoring clinical HIV-1 drug resistance mutations and its population-based surveillance in resource limited settings like India. A primer extension-based process was explored for its ability to interrogate clinically important single nucleotide polymorphisms within the HIV-1 genome thus indicating its potential to be a cost effective, sensitive and specific HIV-1 mutation detection system.

In view of the fact that Hepatitis C virus (HCV) is one of the most significant co-infection that accompanies HIV-1 infection, I effectively investigated methods that can assist in identifying the genotype of this virus. This feature has potential to influence
therapeutic decisions and hence my work is likely to add value to the existing set of tools available for an inclusive management of HIV-1 that include HCV as a co-infection.