The Human Immunodeficiency Virus type 1 (HIV-1) viral envelope glycoprotein that constitutes the outer surface of the virus evolves over the course of infection. Studies have shown that the (C2-V5) region diversifies at an approximate rate of 1% per year in the absence of antiretroviral medications. The envelope glycoprotein variable loops 1 and 2 (V1-V2) expand and add numerous glycosylation sites over the course of infection. These envelope changes arise primarily due to errors during reverse transcription, the high rate of viral replication, and recombination and are associated with progression of disease that leads to Acquired Immune Deficiency Syndrome (AIDS). However, there exists a small population of individuals infected with HIV-1 who remain chronically infected even in the absence of anti-retroviral therapy. Such populations of individuals are referred to as slow progressors. Slow progression indicates presence strong selection pressure. It is believed that the persistence of HIV-1 in the presence of strong humoral immune pressure drives viral envelope to evolve leading to a remarkable increase in its diversity in the course of disease. Envelopes from chronically infected and slow progressing patients are expected to accommodate a few novel amino acids mutations in an effort to evade the host selection pressure. Besides influencing the sensitivity to the host neutralizing-antibody response, these envelope modifications can also potentially affect host cell receptor interactions/usage, replication capacity and also response to diverse entry inhibitors in different target cells.

The present thesis study was carried out to examine the genetic and biological properties of HIV-1 clade C envelopes obtained from slow progressing Indian patients and also compared with those obtained from other stages of disease from other patients. For this study, a panel of functional envelope clones isolated from five chronically infected ART-naïve HIV-1 Indian patients was generated. The plasma of the patients showed considerable breadth in neutralization of several envelope-
pseudotyped viruses. Genetic analyses revealed that while all the envelopes clones obtained, belonged to subtype C; the patient (LT5) harbored quasispecies comprising of pure B, C and B/C recombinants with distinct breakpoints. Phylogenetic analyses of env sequences obtained from the patients showed significant genetic divergences; while in one (LT5), it provided evidence of super infection with genetically distant strains. For dissection of biological properties, the chronic envelopes were compared to existing and previously characterized panel of envelopes representing acute, early (within one year of infection) and late disease stages. We assessed CCR5/CD4 utilization, sensitivities to different broadly neutralizing monoclonal antibodies MAbs, entry inhibitors and lectin Griffithsin[GRFT] having potent anti HIV activity. Our results did not identify a unique phenotype of a disease stage, but uncovered subtle functional differences among the envelopes of different disease stages that may be of biological significance.