9. Recommendations

We are faced with a global HIV-1 pandemic which has taken a significant toll on human longevity and health. The problem is huge and has grown to be so over the last 25 years. Truly it can be said that the efforts of medical, basic and social scientists have been mammoth and met with some degree of success. The war is not won yet but there have been multiple battle successes. The HIV control effort has been multipronged with significant with advances in knowledge of basic biology, immunopathogenesis, natural history, drug development and therapy and the more elusive instrument of battle in the public health arena: ‘The vaccine’.

The experts like Anthony Fauci of the NIH have postulated elegant concepts like sterilizing therapy using a combination of effective ART and immune adjuvant therapeutic vaccine. Such an approach will have a good public health impact as it could reduce the efficiency of transmissions and potential transmitters in the community who undertake risk-behaviour activity. There is also a re-visititation of the earlier view of ART ‘hit early, hit hard’ without waiting for the precipitous drop in CD4 counts. We understand that a prophylactic vaccine is difficult to achieve with this highly mutable infectious agent which attacks and sustains itself successfully in the cardinal cells of the immune system. This scenario forces ‘thinking out of the box’ and looking at getting a handle on the virus early in the course of infection with ART and maintain sustain suppression of the virus with enhancement of the host immune system through vaccination. In the history of vaccination, many successful vaccines do not prevent infection but disease establishment and progression. This pleasant scenario of control of HIV has but ‘a fly in the soup’: the mutable virus is shown to be adept at gaining drug resistance attributes through mutation in the genome, poor regimen compliance by
patients and irresponsible prescription practice by the treating physicians especially in resource poor settings. Drug resistance has been observed in all 5 classes of FDA licensed ART drugs.

In the present scenario emerging in India, multiple groups have shown the problem of both primary and secondary resistance among the clade C strains circulating in different parts of the country. The work embodied in this thesis clearly shows mutations associated with drug resistance in treatment naive and treatment failed individuals. The resistance has been observed for RT and protease inhibitors, though PIs are very infrequently used in India. The NACO regimen is primarily RT inhibitor based. In view of this it would be important to have continuous monitoring of HIV drug resistance. The phenotypic assays should be available at a few specialized laboratories in the country. The genotypic assay should be introduced in many centres with adequate care to quality control with sufficient infrastructure and trained personnel. The sequence data should be submitted to GenBank so that it can be accessed by HIV drug resistance databases and experience with Indian subtype C enriched. Specifically, the newly available bioinformatics tools should be applied for drug discovery targeting the different steps in HIV replication.

The work carried out on genotypic recognition of NS1 (R5) and SI (X4) strains indicates that more work needs to be done on identifying the role of X4 strains emerging among subtype C and its role in pathogenesis of the disease.

Laboratory scientists and infectious disease experts treating HIV patients must work in close collaboration to develop suitable India specific treatment options and monitoring mechanisms.