7. SUMMARY

HIV infection and progression to AIDS and subsequently leading to mortality have been slowed down significantly in the past era due to the potential of HAART regimens. But attaining a status of complete cure seems to be a far horizon though moderate successes have been achieved in vaccine trials such as RV144 study. Thus individuals such as LTNP and EC who have reduced viremia and disease non-progression by natural means have gained importance. Research on various immunological aspects of LTNP and EC might help in understanding the complex nature of immunopathogenesis of HIV. Hence, in the present study, immunological perspectives of disease non-progression in LTNP were compared to that of progressors from which the association and relativity of immune factors in LTNP could be assessed.

- IL-2 expression was not significantly different between LTNP and progressors but their positive correlation with CD4% suggests that LTNP possess better proliferative capability that might have contributed to their better CD4+ T-cell counts.

- IFN-γ expression by T-cells were observed to be higher in LTNP with PVL >2000 copies/mL and negatively correlated with CD4+ T-cell counts. This signifies that in this study, rather than antiviral activity, IFN-γ expression is a sign of enhancing HIV
replication which in turn might result in detrimental inflammation.

- TNF-α expression by CD8- T-cells was also observed more frequently in LTNP than in progressors which is contrasting to other studies. Also, in LTNP, it negatively correlated with CD4+ T-cell count and positively with PVL which proves to be evidence of pro-inflammatory activity. As LTNP cohort involved in this study had disease non-progression for >7 years to >10 years, TNF-α might be a marker of waning immunity in LTNP.

- MIP-1β, in this study had more direct correlation with PVL in both LTNP and progressors. Hence, MIP-1β might be playing significant role in upregulating viral replication rather than an antagonistic approach.

- Lesser activation might have a productive role in controlling viral replication LTNP. Activation rates were much lower in LTNP with PVL <2000 copies/mL suggesting that lesser target or susceptible cells for viral replication might be a beneficial factor in disease non-progression in LTNP.

- T-regs were shown to be significantly lower in LTNP compared to progressors. Inverse correlations between T-regs and CD4+ T-
cell activation rates shows the occurrence of effective balance between the two factors in LTNP thus playing a significant role in disease non-progression. Hence, in this study T-regs play a beneficial role though it might also be responsible for diminished effector functions.

- cTfh-like cells were significantly elevated in LTNP than progressors yet there was no production of bNAb observed in LTNP. It might be due to lesser antigenic stimulus but role of higher proportion of cTfh-like cells in LTNP cohort and its role in B-cell immunity have to be evaluated further.

- There were no differences found in memory B-cells subsets between LTNP and progressors. This might be because differences in memory B-cell subsets were found when the CD4+ T-cell counts were <300 cells/mm$^3$. This study involved participants with CD4+ T-cell count >300 cells/mm$^3$ and hence the differences might not be evident in this study.

- Unlike as observed in cellular expression, the levels of CXCR3 ligand, IFN-γ were lower in LTNP in plasma, which in turn might have influenced the lower IP-10 levels in LTNP thus helping in decreased inflammation rates.
Though there is an absence of statistical significance, lower proportion of levels of TH2 cytokines TNF-α, IL-6, IL-22 were observed in LTNP. Elevated levels of these TH2 cytokines in progressors would have resulted in HIV-related dysfunction that might have influenced the increased disease progression which is not seen in LTNP.

MCP-1 levels were significantly higher whereas, RANTES levels were significantly lower in LTNP. This suggests the need for additional exploration of β-chemokines and their associated factors in disease non-progression in order to derive a significant conclusion.