CHAPTER 6

Conclusions

HIV directly infects various important immune cells such as CD4+ T cells, macrophages and dendritic cells (DCs), leading to destruction and impairment of their functions. Infection with the virus eventually results in progressive deterioration of the immune system, causing "immune deficiency". Infections with influenza A and hepatitis B (HBV) viruses in HIV+ individuals increase serious illness and death of this population. Vaccination is a most effective approach for long-lasting prevention against the diseases caused by these viruses. The effectiveness of both influenza A and HBV vaccination in HIV+ population have been widely investigated, but most of these investigations focused on the humoral immune response. On the contrary, knowledge of the cellular immunity to both influenza and HBV remains limited, even in general HIV− population. The studies in this dissertation aimed to investigate the cellular immune responses after 2009 H1N1 influenza A or HBV vaccination in HIV+ populations.

Firstly, the investigation of cellular immune responses after 2009 H1N1 influenza A vaccination in HIV-infected adults was conducted (chapter 3). This study found no temporal changes in memory-T cell cytokine production in response to *in vitro* influenza vaccine antigen during the three months of study in both HIV+ and HIV− healthy individuals. However, the vaccine induced more expansion of both CD4+ and CD8+ T_{CM} and T_{EM} cells after *in vitro* stimulation with the vaccine in HIV− healthy compared to HIV+ individuals at the end of three months of study. The increases of CD4+ and CD8+ T_{CM} and T_{EM} cells were accompanied by increases in expression of activation marker CD69 and chemokine receptors CCR5 and CXCR3 in HIV− healthy individuals, suggesting that memory T cells in the healthy may more efficiently migrate to the site of infection.

In the second study (chapter 4), we investigated the conserved epitopes-specific memory CD8+ T cells responses in HIV+ children after 2009 H1N1 Influenza A vaccination. Our study found no statistical differences in the frequencies of both total and memory CD8+ T cells that produced cytokines or expressed CD107a in response to the pooled H1N1 influenza A peptides stimulation *in vitro* after vaccinations between groups with different serological responses. This suggests that vaccination with 2009 H1N1 influenza A Panenza® vaccine could not induce conserved-epitope-specific memory CD8+ T cells responses in HIV+ northern Thai children. However, poor immunogenicity of the vaccine itself was also a concern and insufficient coverage of HLA types should be taken into consideration. Comparison of CMI responses between HIV– healthy and HIV+ children is also needed in the future study.

For the third study, we focused on cellular immune responses after different hepatitis B vaccination regimen in HIV-infected Individuals (chapter 5). We found no statistical differences in the frequencies of cytokine-producing and CD107a-expressing of total or memory CD4+ or CD8+ T cells during the 12 months of study among three HIV+ groups. However, we found a more pronounced of TNF-α and IL-2 production from memory CD4+ T cells at 7m after vaccination in healthy controls compared to HIV+ group whom received the same vaccination regimen (the standard dose group). CMI responses in HIV+ participants who received increasing dose and/or frequency were comparable to health individuals. Increasing dose and/or frequency may yield small increase in CMI responses in HIV+ population.

Collectively, we propose that HIV+ individuals might be inferior to generate the effective cellular immune responses against both influenza and HBV vaccination. The impairments of cellular immune responses reveal in the defects of T cells migration to the sites of infection, the generation of conserved-epitope-specific memory CD8+ T cells after influenza vaccination and the production of cytokines of memory CD4+ T cells after HBV vaccination. Our results also indicate that the cellular immune responses to both vaccines do not correlate to the antibody responses. This information may provide valuable perception for future vaccine design to improve cellular immune responses to influenza and HBV vaccination for these populations.