

CHAPTER VI

CONCLUSIONS

Host factors have an important influence in determining the rate of disease progression in HIV-infected individuals. After identification of the role that chemokine receptors (CCR5 and CXCR4) play as major HIV coreceptors, investigators were interested in finding polymorphisms in the coding sequences for the chemokines and chemokine receptors that might confer resistance to HIV infection and/or AIDS. To date, four such mutations have been identified, namely: CCR5 Δ 32, CCR5m303, CCR2-64I, and SDF1-3'A; and they are clearly linked with resistance to, or at least slower progression to AIDS.

The allele frequencies for CCR5 Δ 32 are restricted to Caucasian populations in which they are present at about 10%. They are very rarely found in other ethnic groups. For CCR5m303, the allele frequency of this allele were about 1% in Caucasian and there were some reports shown that this allele were absent in non-Caucasian populations such as in Cambodian and Chinese.

By contrast, the CCR2-64I allele is broadly distributed across human populations, varying in frequency from 10 to 26 % depending on the ethnic group. In Asians, the frequency of this allele varies from 15.5% in the Chinese population to 26.2% in Japanese. In the Thai population, as described in this first report, 15.7 % is allele frequency for this polymorphism, with the 95 % CI for Hardy-Weinberg equilibrium of this allele calculated as 10.7% to 20.8%. These data from the Thai population match very well with the described frequency in the Chinese (Taiwanese) population and are consistent within the ranges of other studies in Asian population (15.5 to 26.2%).

Similarly to CCR5 Δ 32, the allele frequency of SDF1-3'A varies substantially between racial groups. The lowest frequency of this allele has been identified in Africans (3% to 9%) and the highest in Oceanian groups (53.6% to 71.4%). There are

several previous reports that have documented the presence of the SDF1-3'A allele in Asian populations, with a reported frequency ranging from 24.4 to 36.6%; But these studies have not specifically included the Thai population. This study reports the frequency of this allele in a random sample of healthy Thai for the first time. The SDF1-3'A allele frequency was found to be 33.3%. The distribution of genotypes was in agreement with Hardy-Weinberg equilibrium (26.8% to 39.7%). This study shows a high frequency of this allele in Thai people- similar to that which has been described in other south Asian and Japanese groups.

This is the first and largest genetic survey that has been undertaken to examine the frequency of the CCR2-64I and SDF1-3'A alleles in the Thai population. The results document that the frequencies of these alleles in Thai people are not significantly different from those in other Asian populations. Of note, Approximately 13.5 % of Thais showed SDF1-3'A homozygous mutation of which has shown associated with a marked slowing in disease progression if one was HIV infection.

South East Asia, Thailand in particular, has experienced an explosive epidemic of HIV-1. Much important work has been performed upon the role of host genetic factors in the HIV epidemic elsewhere in the world. The discovery of genetic polymorphism that influence HIV-1 infection or pathogenesis has shown striking differences in their distribution between racial groups. It has been important also to examine these alleles in the Thai population and the findings of this study will have implications for the future management of the epidemic both in Thailand and regionally. An understanding of the full biological significance of these alleles will only come from more detailed knowledge of their world-wide distribution and their impact on HIV disease in differing host genetic backgrounds. It is to be hoped that this work has contributed to this field of study and that future work on novel host mutations that important in HIV infection will extended as they are discovered.