VI. SUMMARY

Typing of the HLA class II antigens by serologic method can crudely differentiate HLA-DQ molecules into three types which may not adequately reflect the heterogeneity of the HLA-DQ locus. To determine the association between HLA-DQ alleles and leprosy or subtypes of leprosy, typing of the HLA-DQA1 and HLA-DQB1 alleles employing the polymerase chain reaction and sequence-specific oligonucleotide hybridization (PCR-SSO) methods was performed. This technique can finely distinguish HLA-DQA1 and HLA-DQB1 alleles into nine and seventeen alleles. Genomic DNA of 120 normal controls and 143 leprosy patients belonging to the northern Thai ethnic group was prepared from peripheral blood leukocytes and the polymorphic second exons of the HLA-DQA1 and HLA-DQB1 genes were amplified by PCR. The amplified products were hybridized with ten and seventeen, respectively, each of digoxigenin-labeled HLA-DQA and HLA-DQB SSO probes. The hybridization was visualized by using alkaline phosphatase-conjugated anti-digoxigenin and chemiluminescent AMPPD substrate. Of the possible nine HLA-DQA1 alleles tested for, seven were found. Similarly, eleven out of seventeen HLA-DQB1 alleles were detected. The alleles DQA1*03012, DQA1*0401, DQB1*0503, DQB1*0504, DQB1*0604, DQB1*0605, DQB1*03031, and DQB1*0402 were absent from this population. HLA-DQA1*0102, DQA1*0101, and DQB1*0502 were the most common alleles of these two loci. Interestingly, an unusual HLA-DQB1 allele was detected in three individuals. This represents the HLA-DQB1*0502 allele that hybridizes with the SSO probe 2603. Distribution of the HLA-DQA1 and -DQB1 genotypes of the normal control groups based on the Hardy-Weinberg analysis was in equilibrium. As analyzed by the chi-square test, eleven haplotypes of the HLA-DQA1 and HLA-DQB1 alleles were in strong linkage disequilibrium. All of these haplotypes were previously observed in northern and Shanghai Chinese; only some were detected in Caucasians.

Statistically significant association was not detected between any HLA-DQA1 and HLA-DQB1 alleles with leprosy, tuberculoid subgroup or lepromatous subgroup. When the HLA-DQA1 and -DQB1 alleles were reclassified into three corresponding serologic groups, no association was observed with leprosy or any subgroups of leprosy. The discrepancy between this result with that of Schauf et

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al, who found the association between HLA-DQw1 antigen with tuberculoid leprosy, may be due to the small sample size.

When leprosy patients were classified into four subgroup (TT, BT, BL and LL), still, no association of HLA-DQA1 and -DQB1 alleles with these subgroups was found. This is in contrast to the study of Rani et al. in northern India. The possible explanations are: first, the HLA-DQA1*0103 allele that is associated with leprosy in India is found in a much lower frequency among northern Thais. Second, the association between HLA-DQA1*0102, -DQA1*0103 and -DQB1*0601 and leprosy in northern India may be due to their strong linkage disequilibrium with the allele HLA-DRB1*15. Such linkage disequilibrium may not be present in northern Thai population. Third, northern Thai and northern India populations are of different genetic background and the interaction of these background and HLA molecules may be different. Thus, in northern Thai population, the HLA-DQA1 and -DQB1 alleles is not associated with leprosy or the two subgruops of leprosy. It is possible that other linked genes such as HLA-DR and -DP genes is associated with leprosy in this population.

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