Thesis Title	HLA Class II in Leprosy Patients in Northern Thailand
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ABSTRACT

Mycobacterium leprae (M. leprae), the causative agent of leprosy, is an intracellular pathogen. The leprosy bacillus is virtually non toxic. The manifestation and type of leprosy, both of which develop after infection, are influenced by the T cell mediated immune response that is mounted by the host against *M. leprae*. At one pole, tuberculoid (TT) patients display a positive, acquired cell-mediated immunity and, at the other, lepromatous patients show an absence of specific T-cell response to *M. leprae*. Although the two groups of patients are infected with the same bacteria, they show clinical pathologic differences. Whether there is any genetic factor that might be governing the expression of the disease is interesting. In this study, the distribution of HLA alleles were examined in 145 leprosy patients and 121 normal controls from northern Thai people. The methods of PCR amplification at the polymorphic second exon and sequence specific oligonucleotide (SSO) typing for DRB1,DRB3 and DRB5 were performed.

A set of primers for DRB-generic, DRB1 group specific of DR2, DR4 and DR52-related, and locus-specific of DRB3 were used and followed by hybridization to the PCR products. A panel of 48 DRB SSO probes were hybridized to identify the types and subtypes of DRB alleles. The hybridization was performed with either 5' end labelled ^{32}P T4 polynucleotide kinase or 3' end labelled dig-11-ddUTP terminal deoxynucleotidyl transferase. The tetramethylammonium chloride (TMAC) protocols for prehybridization, hybridization and washing were carried out. The autoradiography of isotopic ^{32}P or chemiluminescent detection of Lumigen PPD was performed on an X ray film for both short and long exposures.

In order to investigate the relationship between HLA and leprosy patients, HLA-DRB1, DRB3, and DRB5 alleles were studied in 145 leprosy patients and compared to 121 ethnically matched controls. HLA-DRB1*1501+1502 was found to be increased significantly in leprosy patients ($\chi2=7.6$, $p=0.006$), as was DRB5*0101 ($\chi2=6.0$, $p=0.014$) due, most probably, to the linkage disequilibrium between alleles of the DRB1 and DRB5 loci. DRB1*(1501+1502) was increased significantly in the frequency of LL and LL+BL patients when compared to normal controls ($\chi2=5.8$, $p=0.016$ and $\chi2=8.0$, $p=0.005$). DRB1*1401 was found to be increased significantly in TT patients when compared to BT patients ($\chi2=6.5$, $p=0.011$). The analysis of HLA-DR allele frequencies in leprosy patients performed in this study, could be beneficial in furthering our understanding of the immunogenetics basis of the pathology of leprosy and perhaps other mycobacterial diseases in Thailand.