

# HLA Diversity and Infections

Pages with reference to book, From 287 To 287

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The genes of the human Major histocompatibility complex (MHC) on the short arm of chromosome 6, play a crucial role in the recognition of “self” from “non-self”. In man this complex is referred to as the Human Leucocyte Antigen (HLA) system. These HLA antigens are grouped as Class I and Class II depending on their distribution on nucleated cells. HLA antigens (three of Class I, HLAs A, B and C and three of Class II, HLAs DR, DP and DQ) bind antigenic peptides for presentation to antigen specific T cells via the T-cell receptor (TCR). The TCR's recognize MHC-peptide complexes on the surface of antigen presenting cells. CD8 positive T-cells recognize Class I complexes and CD4 cells recognize Class II complexes. MHC molecules show variations (Polymorphism) where each HLA antigen has multiple alleles within a given population. Such frequencies are now known for Pakistani populations<sup>1</sup>. These facts together with known infectious diseases association with particular HLA type have generated interest whether this polymorphism of HLA is pathogen driven i.e., adaptation of the human immune system to tackle the various variety of pathogens. A greater diversity of HLAs may protect against infectious disease. It has been shown that people with certain high frequency HLA antigens are less likely to develop disease after infection e.g. HLA-A2 for HTLV-1 and ELI V-1<sup>2</sup> and HLAB53 against severe Malaria<sup>3</sup>. However, many of such studies have been on small number of patients and thus were unable to assess typically low-frequency variants. Convincing evidence comes from study of Class II antigens. HLA DR2 increases susceptibility to leprosy and tuberculosis in Asia<sup>4</sup>. HLAs DR 13 and DR11 are associated with clearance of infection by the hepatitis viruses B and C respectively and DR3 with severe malaria<sup>4</sup>.

The second aspect after polymorphism is the benefits of a state of heterozygosity, i.e., individuals who have two rather than one HLA at each locus at HLAs A, B, C and HLAs DR DP DQ express six different peptides each for both Class I and II on their cell surface. These individuals may generate a stronger immune response than those with only one type of antigen presenting molecule per locus. This advantage has been known in viral diseases specially hepatitis B in terms of class I antigens<sup>5</sup>. Therefore, the combination of HLA variants, polymorphism and heterozygosity offer great diversity and advantage towards handling pathogens. On the other hand, we know that the genetic variation in the infectious pathogen may be significant. Thus these are substantial sequence variations in HIV, CMV, HCV and Malaria, which may change immunogenic epitopes during infections<sup>6</sup>. This viral polymorphism may explain different results in many HLA studies specially in HIV and AIDS patients. Recent studies document the selection process that virus can exert on HLA types and HLA system. The question is which precedes? HLA polymorphism or pathogen polymorphism. The challenge is thus to design vaccines that will allow the host to strike back and effect new pressures on pathogen and viral diversification. The knowledge of HLA frequencies in a given population will thus allow therapeutic as well as preventative options for infectious diseases. In this context tuberculosis, hepatitis B and hepatitis C are three infections which can be addressed in Pakistani population.

## References

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