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The Human Leukocyte Antigen (HLA) System

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ABSTRACT The discovery of Major Histocompatibility Complex (MHC) and its involvement in graft rejection, immune response and the genetic basis of disease associations lead to the birth of this new field of science called Immunogenetics. This field is important not only in basic biomedical research but also in clinical medicine. The growth of this field was further substantiated by the various International Histocompatibility Workshops. Solutions to idiopathic syndromes and autoimmune diseases come from the field of Immunology, Immunogenetics and Molecular biology. In studying the genetic basis of disease susceptibility in human beings, one has to have a different approach because predictive experimental mating cannot be achieved in humans as in animal models; moreover the generation time is longer. One approach is through a study of randomly selected patients and comparing their results with those of controls and the other is through a study of affected families (nuclear or extended) and looking for the mode of inheritance of the disease with relation to genetic markers. Nonetheless the sampling stratification, sample heterogeneity, disease heterogeneity, and age at onset, epidemiological conditions and other socio-biological factors limit these studies. Essentially attempts are to be made to control these parameters and achieve a meaningful conclusion. The current concepts of antigen presentation to immunocompetent cells indicate that antigen processing takes place in the acid environment of the endosomes of antigen presenting cells. Proteolytic degradation of the antigenic proteins results in peptides of different fragments, which are subsequently presented by MHC molecules after they are bound to peptide binding site of the MHC molecules which can bind a variety of peptides having in common, a peptide backbone. These immunogenic peptides (held snugly in the groove by hydrogen bonds between the MHC protein and the peptide backbone) on antigen presenting cells, with the MHC molecule and T-cell receptor on T-cells form a stable trimolecular complex. Thus MHC molecules and alpha beta T-cell receptors or gamma delta T-cell receptor play a major role in the subsequent immune response. The polymorphism of the MHC molecules and T-cell receptor may play an important role in the antigen recognition process. It is possible that a few of the many alleles of a given HLA locus may provide a more stable trimolecular complex than others, thus resulting in a 'high responder status' of an individual than the rest of the alleles. This field of HLA system has been evolving very fast and therefore an updated HLA system review has been provided.

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