

Role of HLA and KIR in Rheumatoid Arthritis and Crohn's Disease

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Synopsis:

The human leucocyte antigen (HLA) loci are the most polymorphic loci in the human genome. The products of these genes present endogenous and exogenous peptides on the cell surface for inspection by T-cells, which recognize and respond to HLA-presented antigens by initiating specific immune responses. Immune responses to infectious pathogens result from the recognition of foreign peptides, while autoimmune diseases result from the recognition of specific self peptides. The nature of the peptides that can be presented to the T-cell receptor by a given HLA molecule is determined by the polymorphic amino acid residues in the peptide binding groove. In addition, specific epitopes on HLA class I molecules serve as ligands for natural killer cell immunoglobulin-like receptors (KIR). Both inhibitory and activating KIR are found on natural killer (NK) and a small percentage of cytotoxic T-cells, where they are important in regulating cell execution and cytokine response. There is diversity in terms of both the number and combination of KIR genes among individuals, as well as extensive allelic polymorphism, all of which could affect the strength and breadth of the immune response. The balance between inhibitory and activating NK receptors and their specific HLA ligands may therefore play an important role in immune related disease.

The specific aims of this study are:

1. Determine the role of HLA and KIR gene and haplotype polymorphism in Rheumatoid Arthritis in a case-control association study.
2. Identify associations between HLA and KIR genetic combinations in Crohn's Disease patients and immuno-phenotypic sub-groups of patients by performing a comprehensive association study using a case/control design.