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Opinion Article

Different Stages of Human Leukocyte Antigen (HLA) and Genetic Variants in Genes

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DESCRIPTION

The Human Leukocyte Antigen (HLA) system or complex is a group of genes on chromosome 6 that encode cell-surface proteins that regulate the immune system. The HLA system is also known as the human version of the Major Histocompatibility Complexes (MHC), which is found in many animals. Human Leukocyte Antigens (HLA) is genes found in Major Histocompatibility Complexes (MHC) that help code for proteins that distinguish self from non-self. They are important in disease and immune defense. They are beneficial to the immune system but can also be harmful. The interaction with complement, the cytotoxic effect of T cells, and cellular humeral immunity are all immune system effects. They also play a role in autoimmunity and are still being studied for their future effects and interactions.

The HLA system is useful in tissue typing, which is the process of analyzing tissues from one person to determine whether they can be successfully transplanted to another. A number of HLA genes have been linked to human diseases such as autoimmune disorders and cancer. MHC class II HLAs (DP, DM, DO, DQ, and DR) present antigens from outside the cell to T-lymphocytes. These antigens stimulate the proliferation of T-helper cells (also known as CD4-positive T cells), which stimulate antibody-producing B-cells to produce antibodies against that specific antigen. Regulatory T cells suppress self-antigens. It is difficult to predict which (fragments of) antigens will be presented to the immune system by a specific HLA type, but technology is improving. Different Human Leukocyte Antigen (HLA) genetic variants in genes of both class I and class II of the human MHC region have been linked to immune-mediated diseases.

Because we are dealing with susceptibility rather than dominant or recessive classical genetic transmission in immune-mediated diseases, the role of HLA variants is frequently unclear, leading researchers to frequently describe the percentage of different alleles without attempting to understand the underlying mechanisms. At the moment, only a few hypotheses have been proposed, such as the epitope-shared thesis in rheumatoid arthritis or the immune systems self-attack driven by pathogen-like antigens. Furthermore, there is a lack of guidelines to assist researchers, particularly clinicians, in dealing with hundreds of HLA alleles and the biological differences between them. As a result, there is an urgent need for research into the development of new guidelines for collecting and managing HLA data, new hypotheses on the mechanisms underlying the pivotal role of HLA variants in disease susceptibility, and reviews on the role of HLA alleles in the development of immune-mediated diseases.

Class I MHC molecules

These are found on the surface of all nucleated cells as trans membrane glycoproteins. An alpha heavy chain is bound to a beta-2 microglobulin molecule in intact class I molecules. The heavy chain is made up of two peptide-binding domains, an Ig-like domain, and a trans membrane region with a cytoplasmic tail. Genes at the HLA-A, HLA-B, and HLA-C loci encode the heavy chain of the class I molecule. T cells expressing CD8 molecules bind to class I MHC molecules. These lymphocytes frequently perform cytotoxic functions, which necessitates their ability to recognize any infected cell. Because every nucleated cell expresses class I MHC molecules, every infected cell can function as an antigen-presenting cell for CD8 T cells (CD8 binds to the nonpolymorphic part of the class I heavy chain). Nonclassical MHC molecules encoded by some class I MHC genes include HLA-G (which may protect the foetus from the maternal immune response) and HLA-E.

Class II MHC molecules

Only professional antigen-presenting cells, thymic epithelium, and activated T cells express class II MHC molecules; most nucleated cells can be induced to express class II MHC molecules by interferon (IFN)-gamma. Class II MHC molecules are made up of two polypeptide chains with a peptide-binding domain, an Ig-like domain, and a transmembrane region with a cytoplasmic tail. Both polypeptide chains are encoded by genes on chromosome 6 in the HLA-DP, -DQ, or -DR regions. T cells that respond to class II molecules express CD4 and are frequently helper cells.

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Class III MHC molecules

Several molecules important in inflammation are encoded by the MHC class III region of the genome, including complement components C2, C4, and factor B; Tumor Necrosis Factor (TNF)-alpha; lymphotoxin; and three heat shock proteins. Individual serologically defined antigens encoded by the HLA system's class I and II gene loci are given standard designations. To identify the gene, alleles defined by DNA sequencing are named, followed by an asterisk, numbers representing the allele group, a colon, and numbers representing the specific allele. Additional numbers are sometimes added after a colon to identify allelic variants that encode identical proteins, and other numbers are added after another colon to denote polymorphisms in introns or 5' or 3' untranslated regions.