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Histocompatibility leukocyte antigens specific antibodies: Characteristics, detection and clinical relevance

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In solid organ transplantations the graft outcomes critically depend on the degree of human leukocyte antigen (HLA) matching between the donor and recipient. Although the cellular component of the immune response to the transplanted tissue plays a key role, the contribution of antibodies should not be underestimated. Highly sensitive technologies such as solid-phase based single antigen assay allow to determine even low concentrations of donor specific antibodies and with a high degree of confidence to predict graft outcomes. Development of anti-HLA antibodies strictly depends on immunogenicity of mismatched HLAs. The latter is defined by fine epitope structure of HLA. Each HLA protein represents a linear sequence of aminoacid residues (AAR) or triplets and the degree of mismatch is assessed as the number of triplets that are not shared between the donor and the recipient. Further investigations of the three dimensional structure of antibody-antigen complexes showed that HLA epitopes could be presented by a group of AARs that are not located beside one another, but rather represent a 3-Å to 5-Å radius patch. These patches have been defined as eplets. Some of eplets include short sequences of AARs, which are equivalent to triplets, whereas, others contain discontinuously located AAR. Further studies demonstrated that area of interaction between complementarity determining region of antibody and HLA is about 900 Å2 and comprises structural and functional epitopes. The former is responsible for binding, whereas the later determine strength of antigen-antibody interaction, which in tern results to conformation changes of antibody and subsequent complement activation.

Biography

Andrew Lobashevsky MD,PhD, D(ABHI)- Diplomat of American Board of Histocompatibility and Immunogenetics is Associate Professor and Histocompatibility Laboratory Director at Department of Medicine of Indiana University and Clarian Health Partners Inc. Dr. Andrew Lobashevsky joined the IU Department of Medicine in December 2004, as the Directory of the Immunology-Histocompatibility Laboratory. Previously, Dr. Lobashevsky was the Co-director of the HLA Laboratory at the University of Alabama at Birmingham Transplant Center, the third largest center in the country. Dr. Lobashevsky received his medical education and postgraduate training at the Department of Immunology and Microbiology of Sechenov's Medical Academy, Moscow, Russia. He had his post-doctoral training in cellular and molecular immunology at the University of Tennessee at Memphis, and received transplant immunology/histocompatibility training at the University of Alabama at Birmingham. The laboratory headed by Dr. Lobashevsky is focused on providing service for the solid organ transplant programs as well as the bone marrow transplant activities of the Hematology/Oncology division at IU.

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