HLA Typing

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Links
[A] https://www.eurotransplant.org/cms/index.php?page=et_manual
[B] http://optn.transplant.hrsa.gov/policiesAndBylaws/policies.asp
[C] http://www.ncbi.nlm.nih.gov/projects/gv/mhc/
[D] http://www.ebi.ac.uk/ipd/imgt/hla/
[E] http://www.allelefrequencies.net/hla6003a.asp
[F] http://hla-net.eu/
[G] http://hla.alleles.org/
[H] http://epregistry.com.br/index/index
[I] http://www.hlamatchmaker.net/

Human leucocyte antigen (HLA) molecules are the principal determinants of graft antigenicity and constitute a formidable barrier to allogeneic organ transplantation.[1] Clinical outcomes after kidney transplantation are particularly strongly associated with the degree of HLA matching between donor and recipient [A] [B]. Here, we collate web-based resources related to the immunobiology and practice of HLA typing of interest to basic scientists and transplant clinicians alike.

The HLA molecules are membrane-bound glycoproteins that bind antigenic peptides for presentation to T cells.[2] According to their structure and function, classical HLA molecules fall into 2 classes: Class I molecules comprise a single peptide-binding, α-polypeptide chain that associates with β_2-microglobulin and an antigenic peptide to form a mature complex; class II molecules are composed of an α- and β-polypeptide, both of which contribute to binding of antigenic peptides. The HLA class I molecules are expressed by most somatic cells, whereas class II molecules are usually only expressed by specialized cell subsets with immunological function. Classic class I and II molecules are genetically encoded within the major histocompatibility complex (MHC) locus on chromosome 6p21.3, which is a region of very high gene density, extreme polymorphism and clustering of genes with related immunological functions.[3] The 3 genes encoding HLA class I molecules, namely, *HLA-A*, *HLA-B*, and *HLA-C*, reside within the class I region alongside 2 clusters of nonclassic class I genes. Genes for the class II molecules, namely, *HLA-DP*, *HLA-DO*, *HLA-DM*, *HLA-DQ*, and *HLA-DR*, are located in the class II region.

Polymorphism is a defining feature of HLA genes.[4] The IMGT/HLA database [C] at the European Bioinformatics Institute serves as an official repository for HLA allele sequences, as well as offering a selection of online tools for categorizing and comparing HLA alleles.[5]

The dbMHC website [D] hosted at NCBI is a publicly accessible database for HLA allele sequence and related clinical data. The catalogue of HLA allele frequencies in diverse human populations is a particularly valuable resource. For reasons that are not fully explained, the overall rate of genetic recombination in the MHC region is lower than that in the rest of the genome; as a result, many HLA alleles exist in marked linkage disequilibrium. Presumably, a felicitous consequence of inheriting HLA genes as "haplotypic blocks" is that identifying a well-matched donor is more probable than it would otherwise be. Usefully, the dbMHC website also lists HLA haplotype frequencies in different racial groups, as does allelefrequencies.net [E][6] and hla-net.eu [F].[7]

Naming of HLA alleles is standardized by the World Health Organization Nomenclature Committee for Factors of the HLA System. In April 2010, the system of HLA nomenclature was changed to accommodate the large number of allelic variants in some families. An accessible source of information about the current naming of HLA alleles is available at hla.alleles.org [G]. This neatly curated website also provides up-to-date lists of recognized HLA alleles and proteins, as well as a convenient nomenclature conversion tool.

At a molecular level, interactions between non-self HLA molecules and T-cell receptors or antibodies are well explained. Much effort has been invested in describing epitopes of HLA-specific antibodies, which are now being systematically named and collated in an online archive at epregistry.com.br [H], which also lists epitope frequencies, epitope-carrying alleles in Luminex panels, and alleles with antibody-verified epitopes.[8] A practical consequence of this work is an algorithm, known as HLAMatchmaker [I], which is now used by Eurotransplant as part of its "acceptable mismatch" program.[9] Assessing "epitope load" might also provide valuable information for selecting organs for nonsensitized recipients or guiding their posttransplant management.[10]

In summary, knowledge of the HLA system and its relevant nomenclature is important for all transplant professionals. Accurate recording of HLA typing information at the highest available resolution is very valuable, especially in the context

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of clinical trials. In addition to the vast specialist literature, there exist many excellent online sources of information about HLA typing and variety of helpful web-based tools.[11]

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