

HLA matching

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Allograft rejection is directed against human leukocyte antigens (HLAs). These are a group of cell surface glycoprotein molecules. HLA molecules are divided into class I (A, B and C) and class II (DR, DP and DQ). Class I molecules are expressed by antigen-presenting cells (APCs) such as dendritic cells and B lymphocytes. HLA molecules are encoded for in the major histocompatibility complex (MHC) on chromosome 6. They are highly polymorphic, i.e. their amino acid sequences differ widely between individuals. To give an example, there are >1000 variants of the HLA-B gene. This genetic variability means that most transplant donors and recipients have different HLA profiles. Donors and transplant recipients are HLA-typed using DNA sequencing. The antigens at HLA-A, -B and -DR are together described as the tissue type. The level of mismatch between the HLA molecules determines the strength of the immune response. Every individual has two copies of each HLA gene and so for each locus (A, B or DR) it is possible to have 0, 1 or 2 mismatched genes. As the number of mismatches increases so does the chance of immune recognition and rejection. The best matched grafts are described as having a mismatch of 0-0-0, i.e. no mismatches at A, B or DR, respectively. A completely mismatched graft would be annotated as a 2-2-2 mismatch. The effects of the different HLA antigens are not uniform. DR mismatches have a more powerful effect than B mismatches, and A mismatches are the least important. The tissue types of potential renal transplant recipients are held by national organisations, such as NHS Blood and Transplant in the UK, and used to allocate donor organs to patients with the lowest level of HLA mismatch.

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