Personalized organ survival strategies based on cellular and molecular information about donor and recipient compatibility in transplantation

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Abstract

Human Leucocyte Antigen (HLA) or human Major Histocompatibility Complex (MHC) molecules are the most polymorphic gene clusters that are involved in immune recognition. Though polymorphic, these genes are inherited as a cluster without much recombination. With the advancement of molecular techniques like high resolution typing of HLA alleles using sequence- specific primer polymerase chain reaction, Flow cytometry, Luminex technology, next generation sequencing, etc., the allelic differences in a cluster of genes can be identified. This helps in getting the haplotype of an individual which in turn help in assessing the longevity of Solid Organ Transplants (SOT). Historically, Antibody-Mediated Reaction (AMR) and Cell- Mediated Reaction (CMR) implicated two discrete ways of immune responses in the individuals including transplant recipients. Conventionally, Complement depended cell cytotoxicity cross-matching, Elispot, Mixed Lymphocyte Culture, etc., are performed for CMR and AMR evaluation. The final rejection of the SOTs is a result of cellular damage. Control of these rejection responses is done by administration of pre- and post- transplantation immunosuppressive drugs that can target AMR as well as CMR. Categorizing the recipients' AMR and CMR is important in this context for assuring the survival of a graft. HLA 'Epitope Matching' is another concern in transplantation immunology which is generally addressed by tissue typing. Allelic difference, binding affinity and level of HLA expression vary from individual to individual which determines the rejection potential. The recent development in identifying the allelic epitope match has gained its momentum through the concept of 'Eplet Matching'. This relies on the presence of triplets of amino acid sequences, Eplets, and its count across a donor and a recipient. Immuno- informatics tools enable peptide interaction study, binding pocket identification, algorithms for eplet count, haplotype of an individual etc. Characterization of individual differences in each rejection episode using biochemical, molecular and cellular markers like creatinine, exosomes, Tregs, etc., is of the prime important observations in assessing the transplant rejection. Therefore, cellular and molecular interactions gathered by the above methods should be categorized for the recipients' thus preventing graft rejection. This information should be conveyed to the clinicians to take appropriate decisions in an organized manner.