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Clinical Significance of Molecular Matching in Kidney Transplantation

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Kidney transplantation stands as the optimal treatment for end-stage renal disease. However, achieving long-term graft survival remains challenging due to immune-mediated rejection. While traditional human leukocyte antigen (HLA) matching has played a pivotal role in donor selection, recent insights the growing importance of epitope matching over antigen matching. Previous studies have shown that an increase in HLA epitope mismatches correlates with an increased risk of dnDSA development, rejection and graft loss. Currently, enumerating molecular mismatches between recipient and donor is promoted to identify patients at higher risk of developing HLA antibodies, for use in organ allocation, and immunosuppression-minimization strategies. A combined approach that baseline alloimmune risk (molecular mismatch and younger age) and evolving risk factors (a history of nonstandard tacrolimus-mycophenolate immunosuppression, T cell–mediated rejection, or nonadherent behavior) may be the most practical approach to dnDSA surveillance. However, it's essential to note that not all epitope mismatches are immunogenic, emphasizing the need to identify the more immunogenic HLA mismatches and clinically relevant donor epitope-specific HLA antibodies. A comprehensive understanding of HLA immunogenicity and its clinical application necessitates validation across diverse cohorts, identification of immunological differences within populations, and the application of evolutionary and functional distance approaches in heterogeneous patient groups. High-resolution HLA typing and epitope analysis also provides a tool for investigating donor-specific antibodies. The presence of certain clinically relevant donor epitope-specific HLA antibodies (DESAs) has been reported to be significantly associated with increased risk of graft loss. By accurately detecting DESAs, clinicians can predict and prevent allograft rejection. However, successful implementation depends on standardized testing methods for epitope characterization and widespread adoption in clinical settings.

Keywords: Molecular matching, HLA, eplet, kidney, transplantation