

ENHANCING DONOR-SPECIFIC ANTIBODY DETECTION IN TRANSPLANTATION: IMPACT OF HIGH-RESOLUTION HLA TYPING VIA NANOPORE SEQUENCING

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Precise HLA matching is essential in transplantation to minimize alloimmune risk and improve graft survival. Donor-specific antibodies (DSAs) are a major cause of antibody-mediated rejection, and their accurate identification relies heavily on high-resolution HLA typing. Traditional typing methods often leave ambiguities that can limit the clinical relevance of post-transplant DSA analysis.

Next-generation sequencing (NGS) for routine high-resolution HLA typing of kidney transplant recipients and donors, covering HLA-A, -B, -C, -DRB1, -DQB1, -DQA1, -DPA1 and -DPB1 loci is routinely implemented in our laboratory. The HLA typing profiles of 27 transplanted patients, were retrospectively re-analyzed, using Oxford Nanopore technology. High Resolution updated HLA typing results were utilised and the impact of high-resolution allele-level information on donor specific antibody assignment and clinical interpretation was assessed.

High Resolution HLA typing resolved allele-level ambiguities inherent in low-resolution HLA typing, enabling more precise identification of donor-specific antibodies (DSAs). In 22% of patients, a number of antibodies that were previously reported as DSAs based on low-resolution donor typing were reclassified as non-donor-specific when high-resolution NGS data became available. This reclassification may in certain have significant clinical implications, impacting decisions related to biopsy interpretation, immunosuppression management, and immunologic risk stratification.

Misinterpreting DSAs due to typing ambiguities can lead to incorrect risk assessments for antibody-mediated rejection. High-resolution HLA typing significantly improves the accuracy of post-transplant DSA interpretation, leading to better-informed clinical decisions, supports personalized immunosuppression strategies, and ultimately enhances long-term graft outcomes.

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