EXPANDING THE HLA ALLELE REPERTOIRE: 77 NEW VARIANTS IN THE CONTEXT OF HEMATOPOIETIC STEM CELL AND SOLID ORGAN DONOR MATCHING

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The objective of this study was to present 77 novel HLA alleles and assess their significance in selecting the most suitable donor for transplantation.
Between 2021 to the present, 4,860 samples from patients who were candidates for HSCT/SOT and their respective unrelated donors were analyzed. HLA genotyping was performed at 11 loci (HLA-A,-B,-C,-DRB1,-DRB3/4/5,-DQA1,-DQB1,-DPA1,-DPB1) using commercial kits (CareDX/GenDx). Sequencing was conducted on MiSeq platform, with allele assignment via AlloSeq Assign and NGSengine.
Comparison with the IPD-IMGT/HLA Database revealed 77 novel HLA alleles. Most were identified in class I (45/77; 58.44%), with 12, 15 and 18 found in HLA-A, -B and -C, respectively. The remaining alleles (32/77; 41.6%) were identified in class II: HLA-DRB1 (1), -DQA1 (3), -DQB1 (19), -DPA1 (8), and -DPB1 (1). The majority (72/77; 93.51%) comprised single-nucleotide (nt) substitutions, while 5/77 (6.49%) involved multiple nt changes. Specifically, 7 were located in the 5'UTR, 6 in 3'UTR, 49 in intronic, and 15 in exonic regions. Exonic variants comprised one synonymous mutation characterized by a silent base substitution with no change in the amino acid sequence. The remaining 14 were non-synonymous mutations, 4 of which involved polymorphisms in exons encoding the peptide-binding groove, potentially eliciting different immune responses. Among novel alleles, 2 null variants (HLA-A and -DRB1) were identified, resulting from substitution/insertion that caused frameshifts and introduced premature stop codons. By exploring their potential involvement in allo-recognition and their impact on transplant success, these findings contribute to the precise selection of donor-recipient pairs, thereby optimizing transplant outcomes.

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