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Characterization of the novel *HLA-DPB1*11:01:06* allele by sequencing-based typing

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*HLA-DPB1*11:01:06* differs from *HLA-DPB1*11:01:01:01* by one nucleotide substitution in codon 21 in exon 2.

KEYWORDS

HLA, *HLA-DPB1*11:01:06*, novel allele, sequencing-based typing

We report here a novel *HLA-DPB1*11:01* allele, now named *DPB1*11:01:06* that carries one nucleotide substitution in exon 2 when compared to the *DPB1*11:01:01:01* allele, identified in a volunteer bone marrow donor. The HLA typing was performed using Next Generation Sequencing (AllType NGS, One Lambda, Canoga Park, CA) on the Ion S5 system platform (ThermoFisher Scientific, Waltham, MA),[1] from exons 2 to 5. The reads were analyzed using the TypeStream Visual Software version 2.1 (One Lambda). This donor was found to have a new *DPB1*11:01* allele and was consequently typed *A*02:01*, *30:02*; *B*18:01*, *44:03*; *C*05:01*, *16:01*; *DRB1*03:01*, *07:01*; *DRB3*02:02*; *DRB4*01:01*; *DQA1*02:01*, *05:01*; *DQB1*02:01*, *02:02*; *DPA1*01:03*, *02:01*; *DPB1*11:01:06*, *104:01:01*. Using the IPD-IMGT/HLA Database,[2] nucleotide sequence alignment with HLA-DPB1 alleles shows that this new allele has one nucleotide change from *DPB1*11:01:01:01* in codon 21 in exon 2, where A → G, (ACA → ACG, Figure 1), not resulting in a coding change. This nucleotide change was confirmed using other NGS reagents provided by GenDX NGSgo-MX6-1 (Utrecht, Nederlands) run on the Illumina MiSeq system (San Diego, CA) and analyzed with the NGSEngine software (GenDX, version 2.26). We were confident in the phasing as the sample displayed a mean read length of 304 base pairs over all the loci, the mismatched G base was attributed 139 times to the new *HLA-DPB1*11:01:06* allele and can be only attributed to this allele because it was possible to discriminate

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AA Codon                          10                  15                  20                  25
DPB1*11:01:01:01    AG AAT TAC GTG TAC CAG TTA CGG CAG GAA TGC TAC GCG TTT AAT GGG ACA CAG CGC TTC CTG GAG AGA TAC ATC
DPB1*11:01:06       -- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --G --- --- --- --- --- --- --- ---

AA Codon             30                  35                  40                  45                  50
DPB1*11:01:01:01    TAC AAC CGG CAG GAG TAC GCG CGC TTC GAC AGC GAC GTG GGA GAG TTC CGG GCG GTG ACG GAG CTG GGG CGG CCT
DPB1*11:01:06       --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon             55                  60                  65                  70                  75
DPB1*11:01:01:01    GCT GCG GAG TAC TGG AAC AGC CAG AAG GAC CTC CTG GAG GAG AGG CGG GCA GTG CCG GAC AGG ATG TGC AGA CAC
DPB1*11:01:06       --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon             80                  85                  90
DPB1*11:01:01:01    AAC TAC GAG CTG GAC GAG GCC GTG ACC CTG CAG CGC CGA G
DPB1*11:01:06       --- --- --- --- --- --- --- --- --- --- --- --- --- -
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FIGURE 1 Alignment of the sequence of exon 2 of *HLA-DPB1*11:01:06* allele with the sequence of *HLA-DPB1*11:01:01:01*. Dashes indicate nucleotide identity with the *HLA-DPB1*11:01:01:01* allele. Numbers above the sequence indicate codon position.

from the associated *HLA-DPB1*104:01:01:01* allele by virtue of 4 variant positions each distant by less than 100 base pairs. HLA typing by Luminex reverse sequence-specific oligonucleotide (SSO) was performed (One Lambda Labtype, Canoga Park, CA).[3] With this assay (lot 010, catalog RSSO2P_010_02), the most likely HLA-typing of the patient was *DPB1*11:01*, *104:01* without any bead modification. Indeed the IPD-IMGT/HLA Database 3.50.0 release describe no other HLA-DPB1 alleles displaying a ACG sequence in codon 21, explaining why the manufacturer did not include probes targeting this codon. The nucleotide sequence of the new allele has been submitted to the GenBank database (Accession No. OP393479) and to the IPD-IMGT/HLA Database (Submission No. HWS10062888). The name *DPB1*11:01:06* has been officially assigned by the WHO Nomenclature Committee for Factors of the HLA System in September 2022. This follows the agreed policy that, subject to the conditions stated in the most recent Nomenclature Report,[4] names will be assigned to new sequences as they are identified. Lists of such new names will be published in the following WHO Nomenclature Report.

AUTHOR CONTRIBUTIONS

Marine Cargou and Jonathan Visentin contributed to the design of the study. Marine Cargou and Jonathan Visentin participated in the writing of the paper. Marine Cargou, Vincent Elsermans, Isabelle Top, Elodie Wojciechowski and Jonathan Visentin participated in the performance of the research. Marine Cargou, Vincent Elsermans, Isabelle Top, Elodie Wojciechowski and Jonathan Visentin participated in data analysis. Vincent Elsermans, Isabelle Top and Elodie Wojciechowski were involved in critical revision of the manuscript.

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CONFLICT OF INTEREST

The authors confirm that there are no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions. The sequence is freely available in the IPD-IMGT/HLA database.

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