Characterization of the novel *HLA-DPB1*1348:01* allele by sequencing-based typing

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*HLA-DPB1*1348:01* differs from *HLA-DPB1*14:01:01:01* by one nucleotide substitution in codon 147 in exon 3.

KEYWORDS

HLA, *HLA-DPB1*1348:01*, novel allele, sequencing-based typing

We report here a novel HLA-DPB1 allele, now named *DPB1*1348:01* that carries one nucleotide substitution in exon 3 when compared with the *DPB1*14:01:01:01* 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 allele and was consequently typed *A*02:01*, *29:02*; *B*18:01*, *44:02*; *C*05:01*, *07:01*; *DRB1*04:01*, *11:04*; *DQA1*03:03*, *05:05*; *DQB1*03:01*, *03:01*; *DPA1*01:03*, *02:01*; *DPB1*04:01*, *1348:01*. 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*14:01:01:01* in codon 147 in exon 3, where G → T, resulting in a new protein (CGT → CTT, Arginine → Leucine, Figure 1). This nucleotide change was confirmed using other NGS reagents provided by Immucor (Mia Fora NGS Flex, Norcross, GA) run on the Illumina MiSeq system (San Diego, CA) and analyzed with the Mia Fora Flex software (Immucor, version 5.1). We were confident in the phasing as the sample displayed a mean read length of 333 base pairs over all the loci, the mismatched T base was attributed 1342 times to the new *HLA-DPB1*1348:01* allele and can be only attributed to this allele because it was possible to discriminate from the associated *HLA-DPB1*04:01:01:01* allele by virtue of 4 variant positions each distant by less than 100 base pairs. HLA typing by Luminex reverse sequence-specific oligonucleotide (SSO)

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AA Codon                 95                 100                105                110                115
DPB1*14:01:01:01    TC CAG CCT AAG GTG AAC GTT TCC CCC TCC AAG AAG GGG CCC CTG CAG CAC CAC AAC CTG CTT GTC TGC CAC GTG
DPB1*1348:01        -- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon                120                125                130                135                140
DPB1*14:01:01:01    ACA GAT TTC TAC CCA GGC AGC ATT CAA GTC CGA TGG TTC CTG AAT GGA CAG GAG GAA ACA GCT GGG GTC GTG TCC
DPB1*1348:01        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon                145                150                155                160                165
DPB1*14:01:01:01    ACC AAC CTG ATC CGT AAT GGA GAC TGG ACC TTC CAG ATC CTG GTG ATG CTG GAA ATG ACC CCC CAG CAG GGA GAC
DPB1*1348:01        --- --- --- --- -T- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon                170                175                180                185
DPB1*14:01:01:01    GTC TAC ATC TGC CAA GTG GAG CAC ACC AGC CTG GAC AGT CCT GTC ACC GTG GAG TGG A
DPB1*1348:01        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- -
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FIGURE 1 Alignment of the sequence of exon 3 of *HLA-DPB1*1348:01* allele with the sequence of *HLA-DPB1*14:01:01:01*. Dashes indicate nucleotide identity with the *HLA-DPB1*14:01:01:01* allele. Numbers above the sequence indicate codon position.

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*04:01, 14:01* without any bead modification. Indeed the IPD-IMGT/HLA Database 3.50.0 release describe no other HLA-DPB1 alleles displaying a CTT sequence in codon 147, explaining why the manufacturer did not include probes targeting this codon. The analysis of the localization of this amino-acid and its antibody accessibility with the pHLA3D database[4] indicated that this amino-acid is located out of the peptide binding groove while it is surface accessible. Then, Arginine and Leucine are amino-acids having different physico-chemical properties, a transplanted organ from a donor expressing the *HLA-DPB1*1348:01* allele could lead to a humoral allosensitization which cannot be detected by current solid-phase assays. In case of a suspicious antibody-mediated rejection, only the use of donor's cells to perform a retrospective crossmatch could allow the diagnosis. The nucleotide sequence of the new allele has been submitted to the GenBank database (Accession No. ON862913) and to the IPD-IMGT/HLA Database (Submission No. HWS10062026). The name *DPB1*1348:01* has been officially assigned by the WHO Nomenclature Committee for Factors of the HLA System in July 2022. This follows the agreed policy that, subject to the conditions stated in the most recent Nomenclature Report,[5] 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, Mamy Ralazamahaleo and Jonathan Visentin participated in the performance of the research. Marine Cargou, Vincent Elsermans, Isabelle Top, Mamy Ralazamahaleo and Jonathan Visentin participated in data analysis. Vincent Elsermans, Isabelle Top and Mamy Ralazamahaleo were involved in critical revision of the manuscript.

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CONFLICT OF INTEREST

The authors declare 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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