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NEW ALLELE ALERTS

HLA Immune Response Genetics WILEY

The novel *HLA-DQB1*03:445* allele was identified in two unrelated bone marrow donors from Russia

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*HLA-DQB1*03:445* has one nucleotide change from *HLA-DQB1*03:03:02:01* at nucleotide 692.

KEYWORDS
HLA-A, HLA-DQB1*03:445, new HLA allele, NGS

HLA is well known as a highly polymorphic genetic system. Currently, more than 2000 HLA-DQB1 alleles have been identified according to the latest version of IPD-IMGT/HLA Database.[1] We detected the *HLA-DQB1*03:445* allele in our routine HLA typing practice using a next-generation sequencing (NGS).

The blood samples were obtained from two unrelated potential donors of hematopoietic stem cells recruited by National bone marrow donor registry named after Vasya Perevoshchikov. Genomic DNA was isolated from peripheral blood using a QIAcube HT System (Qiagen, Germany). HLA-A, -B, -C, -DRB1, -DQB1, and -DPB1 typing was performed by next generation method using the HoloType HLA kits (Omixon, Inc. Budapest, Hungary) and NGSgo (GenDX, Netherlands). The library was sequenced by the MiSeq reagent kit v.2 and

(A)

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AA Codon              190                 195                 200
DQB1*03:03:02:01    GG GCT CAG TCT GAA TCT GCC CAG AGC AAG ATG CTG AGT GGC ATT GGA
DQB1*03:445         -- --- --- --- --- --- --- --- --- --- -C- --- --- --- --- ---

AA Codon           205                 210                 215                 220
DQB1*03:03:02:01   GGC TTC GTG CTG GGG CTG ATC TTC CTC GGG CTG GGC CTT ATT ATC CAT
DQB1*03:445        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon                        225
DQB1*03:03:02:01   CAC AGG AGT CAG AAA G
DQB1*03:445        --- --- --- --- --- -
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(B)

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AA Pos.                 190         200         210         220
DQB1*03:03:02:01   QNPIIVEWRA QSESAQSKML SGIGGFVLGL IFLGLGLIIH HRSQKGLLH
DQB1*03:445        ---------- --------T- ---------- ---------- ---------
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FIGURE 1 Sequence alignment of *HLA-DQB1*03:445* compared to the most homologous allele *HLA-DQB1*03:03:02:01*, dashes show identity to *DQB1*03:03:02:01*. (A) The DNA sequence of *HLA-DQB1*03:445* is identical *HLA-DQB1*03:03:02:01* in exon 4 (shown here) except in codon 199 where ATG of *DQB1*03:03:02:01* is substituted by ACG in *DQB1*03:445*. (B) The nucleotide substitution leads one amino acid replacement where methionine (M) of *DQB1*03:03:02:01* is substituted by a threonine (T) in *DQB1*03:445*

MiSeq instrument (Illumina, USA). Analysis of the results was carried out using software provided by manufacturers of library preparation kits: NGSengine (GenDX, Netherlands) and HLA Twin (Omixon, Inc. Budapest, Hungary).

The new sequence has one nucleotide change when compared with the most closely related allele, *HLA-DQB1*03:03:02:01*, in exon 4 where T > C (codon 199 ATG- > ACG) resulting in a coding change, methionine is changed to threonine (Figure 1). Nucleotide numbering was obtained by alignment to the reference sequence provided by the IPD-IMGT/HLA Database.[1] The novel variant was found in two unrelated donors. The extended HLA typing of the two donors in which the novel allele was determined was: *HLA-A*25:01:01G, 32:01:01G; C*02:02:02G, 12:03:01G; B*18:01:01G, 40:02:01G; DRB1*07:01:01G, 07:01:01G; DQB1*02:01:01G, 03:445* and *HLA-A*02:01:01G, 03:01:01G; C*03:03:01G, 07:04:01G; B*44:02:01G, 55:01:01G; DRB1*07:01:01G, 08:01:01G; DQB1*03:445, 04:02:01G*.

We report here the identification of the new HLA-DQB1 allele, officially designated as *HLA-DQB1*03:445* for by the World Health Organization (WHO) Nomenclature Committee Factors of the HLA System in October 2020.[2] The nucleotide sequence has been submitted to GenBank with accession number MT658793 and to the IPD-IMGT/HLA Database with accession number HWS10060431.

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CONFLICT OF INTEREST

The authors have declared no conflicting interests.

AUTHOR CONTRIBUTIONS

Shamil Nizamov participated in the performance of the research and participated in data analysis. Elena Shagimardanova and Anastasiia Ananeva contributed to the design of the study and participated in the writing of the article. All authors read and approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Robinson J, Barker DJ, Georgiou X, Cooper MA, Flicek P, Marsh SGE. IPD-IMGT/HLA database. *Nucleic Acids Res*. 2020; 48:D948-D955.
2. Marsh SGE, Albert ED, Bodmer WF, et al. Nomenclature for factors of the HLA system. *Tissue Antigens*. 2010;75:291-455.

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