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NEW ALLELE ALERT

HLA Immune Response Genetics WILEY

The novel *HLA-B*39:199* allele identified in a candidate bone marrow donor

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*HLA-B*39:199* differs from *HLA-B*39:10:01* by a G → A substitution in exon 5 in codon 282.

KEYWORDS
HLA, *HLA-B*39:199*, new allele, next generation sequencing, transplantation

1 | INTRODUCTION

HLA-B is the most polymorphic locus within the HLA family of genes. According to the latest release of the IPD-IMGT/HLA Database, 37,516 HLA alleles have been identified, 9,573 of which are HLA-B alleles (Release 3.54.0, October 2023).[1] The IPD-IMGT/HLA Database can be accessed via the World Wide Web at: www.ebi.ac.uk/ipd/imgt/hla. Utilizing the power of next generation sequencing (NGS) during the HLA typing of a candidate bone marrow donor of Turkish origin we discovered a novel HLA-B allele that was designated by the World Health Organization (WHO) Nomenclature Committee for factors of the HLA System as *HLA-B*39:199*.

Genomic DNA was isolated from the peripheral blood sample of a bone marrow donor candidate using an automatic extractor according to the manufacturer's instructions (EZ1® Advanced XL Qiagen). The HLA typing was performed using the NGSgo-MX6-1 next generation sequencing kit of GenDx (Utrecht, The Netherlands) on the Illumina MiniSeq platform (San Diego, California, CA, USA). The data analysis was carried out utilizing the NGSengine software version 2.29 (GenDx) and IPD-IMGT/HLA Database version 3.51.

The NGS-based HLA-B genotyping exhibited an irregular reaction pattern that did not correspond to any of the so far described HLA-B alleles. The sequencing data suggested the potential presence of a novel allele. The novel allele *HLA-B*39:199* is an exonic variant of *HLA-B*39:10:01*, differing by a single nucleotide polymorphism (SNP) within exon 5 at position 1956G > A in the gDNA sequence. This nucleotide change results in one amino acid substitution in residue 282 from Valine to Isoleucine (Figure 1). Complete HLA typing of this donor including the new allele was *HLA-A*02:01:01:01, 03:02:01:01*; *-B*39:199, 44:02:01:01*; *-C*12:03:01:01, 16:04:01:01*; *-DRB1*04:02:01, 11:01:02:01*; *-DQB1*03:02:01:01, 05:01:01:02*; *-DPB1*04:01:01:41, 104:01:01:01*.

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AA Codon                          280                 285                 290                 295
B*39:10:01      AG CCA TCT TCC CAG TCC ACC GTC CCC ATC GTG GGC ATT GTT GCT GGC CTG GCT GTC CTA GCA GTT GTG GTC ATC
B*39:199        -- --- --- --- --- --- --- A-- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon
B*39:10:01      GGA GCT GTG GTC GCT GCT GTG ATG TGT AGG AGG AAG AGT TCA G
B*39:199        --- --- --- --- --- --- --- --- --- --- --- --- --- --- -
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FIGURE 1 Alignment of the exon 5 nucleotide sequence of the *HLA-B*39:199* allele with the sequence of *HLA-B*39:10:01*. Dashes indicate nucleotide identity with the *HLA-B*39:10:01* allele. The numbers above the sequence indicate the codon positions. Codon 282 of *HLA-B*39:199* demonstrates a substitution of GTC by ATC causing a substitution of the amino acid Valine by Isoleucine.

The sequence of this newly identified HLA-B allele was deposited in the GenBank and IPD-IMGT/HLA database with submission numbers OQ974172 and HWS10066417, respectively. The name *B*39:199* has been officially assigned by the WHO Nomenclature Committee for Factors of the HLA System in June 2023.[2] This follows the agreed policy that, subject to conditions stated in the most recent Nomenclature Report, names will be assigned to new sequences as they are identified.[3]

The discovery of this new allele contributes to the understanding of HLA diversity and its implications in organ and stem cell/bone marrow transplantation.

AUTHOR CONTRIBUTIONS

Sebahat Usta Akgul designed the experiment and revised the manuscript, Talin Catalbasyan performed the laboratory analysis and submitted the new sequence to the IMGT/HLA database and Genbank, and Mahdis Borjkhani and Demir Kaan Demir wrote the paper. Caner Süsal critically read and revised the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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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