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NEW ALLELE ALERT

HLA Immune Response Genetics WILEY

Characterization of the novel *HLA-B*40:539* allele by sequencing-based typing

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*HLA-B*40:539* differs from *HLA-B*40:01:01* by one nucleotide substitution in codon 46 in exon 2.

KEYWORDS

HLA, *HLA-B*40:539*, novel allele, sequencing-based typing

We report here a novel *HLA-B*40* allele, *B*40:539* that carries one nucleotide substitution in exon 2 when compared to the *B*40:01:01* allele, identified in a volunteer unrelated hematopoietic stem cell donor. The HLA typing was performed using Next Generation Sequencing reagents provided by Protrans (Protrans N5, Hockenheim, Germany) run on the Miseq system platform (Illumina, San Diego, CA). The reads were analyzed using the SeqPilot software (version 5.2.0) (JSI Medical Systems, Ettenheim, Germany). The subject was found to have a new *B*40* allele and was consequently typed *A*02:01, 68:02*; *C*03:04, 08:02*; *B*14:02, 40:539*; *DRB1*01:02, 13:01*; *DQB1*05:01, 06:03*; *DPB1*13:01, 13:01*. Using the IPD-IMGT/HLA Database,[1] nucleotide sequence alignment with *HLA-B* alleles shows that this new allele has one nucleotide change from *B*40:01:01* in codon 46 of exon 2, where G → C resulting in a new protein (GAG → GAC, Glutamic acid → Aspartic acid, Figure 1). This polymorphism had previously been described in only

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AA Codon                    5                  10                  15                  20                  25
B*40:01:01      GC TCC CAC TCC ATG AGG TAT TTC CAC ACC GCC ATG TCC CGG CCC GGC CGC GGG GAG CCC CGC TTC ATC ACC GTG
B*40:539        -- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon                    30                 35                  40                  45                  50
B*40:01:01      GGC TAC GTG GAC GAC ACG CTG TTC GTG AGG TTC GAC AGC GAC GCC ACG AGT CCG AGG AAG GAG CCG CGG GCG CCA
B*40:539        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --C --- --- --- ---

AA Codon                    55                 60                  65                  70                  75
B*40:01:01      TGG ATA GAG CAG GAG GGG CCG GAG TAT TGG GAC CGG GAG ACA CAG ATC TCC AAG ACC AAC ACA CAG ACT TAC CGA
B*40:539        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon                    80                 85                  90
B*40:01:01      GAG AGC CTG CGG AAC CTG CGC GGC TAC TAC AAC CAG AGC GAG GCC G
B*40:539        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- -
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FIGURE 1 Alignment of the sequence of exon 2 of *B*40:539* with the sequence of *B*40:01:01*. Dashes indicate nucleotide identity with the *HLA-B*40:01:01* allele. Numbers above the sequence indicate codon position.

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one other *HLA-B* allele. This nucleotide change was confirmed using DNA sequencing reagents provided by Protrans (Protrans S4 mono allelic SBT kits, Hockenheim, Germany) run on the ABI 3730xl (Applied Biosystems, Foster City, CA). Data were analyzed with SeqPilot software (version 5.2.0). Sequencing was performed in both directions (forward and reverse) for exons 2, 3, and 4. The nucleotide sequence of the new allele has been submitted to the GenBank database (accession number OK236546) and to the IPD-IMGT/HLA Database (Submission No. HWS10065787). The name *B*40:539* has been officially assigned by the WHO Nomenclature Committee for Factors of the HLA System in April 2023. This follows the agreed policy that, subject to the conditions stated in the most recent Nomenclature Report,[2] 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.

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CONFLICT OF INTEREST STATEMENT

The authors confirm that there are 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. The sequence is freely available in the IPD-IMGT/HLA Database.

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