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A novel null-allele, *HLA-B*35:574N*, containing a mutation in the start-codon

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*HLA-B*35:574N* contains a single nucleotide substitution at nucleotide position 2 (ATG to ACG).

KEYWORDS
HLA-B null allele, next generation sequencing (NGS)

To date, more the 300 HLA-B null-alleles are listed in the IPD-IMGT/HLA Database.[1] Here, we report on a novel *HLA-B*35* null allele, *HLA-B*35:574N*, which has been identified in a 34-year-old female individual. The full HLA-typing was *HLA-A*02:01*, *03:01*; *-B*35:574N*, *47:01*; *-C*04:01*, *06:02*; *-DRB1*13:03*, *14:01*; *-DQB1*02:02*, *05:03*.

NGS was carried out using the NGSgo®-MX6 sequencing kit according to manufacturer's recommendations and sequenced on an Illumina MiSeq platform. Data analysis was performed by the NGSengine software Version 2.23 (GenDx, the Netherlands).

Confirmatory typing was performed by NGS using the ProTrans NGS Kit for seven loci (ProTrans Medical Diagnostics, Hockenheim, Germany) according to manufacturer's recommendations and sequenced on an Illumina MiSeq platform. For allele assignment, the HiType software (Inno-Train, Kronberg, Germany) was used based on the most recent HLA database.

The observed polymorphism affects the START-codon -24 resulting in an amino acid change from methionine to threonine. One might speculate that this alteration leads to the use of alternative START-codon and translation of non-functional protein (Figure 1). However, this assumption would require further expression studies on the protein level.

The nucleotide sequence of the novel allele was submitted to GenBank database and accession numbers OP559477 and HWS10064267 were assigned.[1] The name *B*35:574N* has been officially assigned by the WHO

```
aa codon:          -24             -20                 -15                 -10                  -5
HLA-B*35:01:01:    ATG CGG GTC ACG GCG CCC CGA ACC GTC CTC CTG CTG CTC TGG GGG GCA GTG GCC CTG ACC GAG ACC TGG GCC G
HLA-B*35:574N:     -C- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- -
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FIGURE 1 Alignment of the sequence of exon 1 of *HLA-B35:574N* with the sequence of *HLA-B*35:01:01*. Dashes indicate nucleotide identity. Numbers above indicate codon numbers

Nomenclature Committee for Factors of the HLA System in November 2022. 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.

AUTHOR CONTRIBUTIONS

Mirzokhid Rakhmanov, Martin Bernheiden and Murielle Verboom carried out NGS data acquisition, analyzed and interpreted the NGS data. Florian Emmerich and Mirzokhid Rakhmanov analyzed data and submitted the allele sequence to GenBank. Maike Hofmann provided specimen used for analysis. Mirzokhid Rakhmanov and Florian Emmerich wrote the manuscript. All authors have read and approved the final 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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Detection of the *HLA-B*40:02:03* allele, a variant of *HLA-B*40:02:01:01*, in a Taiwanese individual

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One nucleotide substitution in codon 67 of *HLA-B*40:02:01:01* results in a novel allele, *HLA-B*40:02:03*.

KEYWORDS

HLA, *HLA-B*40:02:03*, novel allele, sequence-based typing, Taiwanese

Using a sequence-based typing (SBT) method we detected the *HLA-B*40:02:03* allele in a Taiwanese individual in our routine HLA typing practice. The DNA material extracted from peripheral blood was subjected to HLA genotyping for HLA-A, -B and -DRB1 loci using commercial PCR-SBT kits (TBG, Medigen Biotechnology, Taipei, Taiwan, Republic of China).