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NEW ALLELE ALERT

The Novel HLA-A*02:1195N Null Allele Identified by Next-Generation Sequencing

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ABSTRACT

HLA-A*02:1195N differs from HLA-A*02:01:01:01 by one nucleotide substitution in exon 4, at gDNA position 1843 (G>A).

The number of HLA alleles continues to increase as Next Generation Sequencing is implemented worldwide. More than 8000 HLA-A alleles, including 449 Null HLA-A alleles are currently listed in the IPD-IMGT/HLA Database (Version 3.59 2025–01) [1]. We describe here a novel null HLA-A allele that was identified in a Belgian kidney transplant recipient. Genomic DNA was extracted from peripheral blood using a commercial Maxwell blood DNA extraction kit (Promega, BE). High resolution HLA typing was performed using next generation sequencing (NGSgo-MX11-3, GenDX, Utrecht, the Netherlands) on the MiSeq system platform (Illumina, USA). Data were analysed by NGSengine software and compared with the IPD-IMGT/HLA Database [2]. The sequencing data showed a best match to the A*02:01:01:01 allele although differing by one mismatch in exon 4 at gDNA position 1843. This substitution resulted in a premature stop codon (TAG) in position 274, making this a null allele (Figure 1). The substitution was exclusively present in the reads assigned to the new A*02:1195N allele and not to the A*02:01 allele also present in the patient. The complete HLA typing of the patient with this novel allele was: HLA-A*02:01,

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AA Codon                                    185                 190                 195                 200
A*02:01:01:01                          AC GCC CCC AAA ACG CAT ATG ACT CAC CAC GCT GTC TCT GAC CAT GAA GCC ACC CTG
A*02:1195N                             -- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon                205                 210                 215                 220                 225
A*02:01:01:01      AGG TGC TGG GCC CTG AGC TTC TAC CCT GCG GAG ATC ACA CTG ACC TGG CAG CGG GAT GGG GAG GAC CAG ACC CAG
A*02:1195N         --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon                230                 235                 240                 245                 250
A*02:01:01:01      GAC ACG GAG CTC GTG GAG ACC AGG CCT GCA GGG GAT GGA ACC TTC CAG AAG TGG GCG GCT GTG GTG GTG CCT TCT
A*02:1195N         --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon                255                 260                 265                 270                 275
A*02:01:01:01      GGA CAG GAG CAG AGA TAC ACC TGC CAT GTG CAG CAT GAG GGT TTG CCC AAG CCC CTC ACC CTG AGA TGG G
A*02:1195N         --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- -A- -
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FIGURE 1 | Comparison of the exon 4 sequences for the HLA-A*02:01:01:01 and HLA-A*02:1195N alleles, which differ at codon 274 (TGG>TAG). Dashes indicate nucleotide sequence identity to HLA-A*02:01:01:01 allele. The numbers above the sequence indicate the codon position.

02:1195N; -B*15:01, 44:02; -C*03:03, 05:01; -DRB1*04:01, 13:01; -DRB3*01:01, -DRB4*01:03; -DQA1*01:03, 03:03; -DQB1*03:01, 06:03; -DPA1*01:03; -DPB1*02:01, 03:01.

The nucleotide sequence of the novel HLA-A*02:1195N allele has been submitted to the GenBank database (accession number PP574991) and IPD-IMGT/HLA Database (submission ID HWS10069920). The name A*02:1195N has been officially assigned by the WHO Nomenclature Committee for Factors of the HLA System in October 2024. 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

Justine Schmitt contributed to the design of the study and data analysis. André Gothot participated in critical revision of the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are openly available in IPD-IMGT/HLA Database at https://www.ebi.ac.uk/ipd/hla/, reference number HWS10069920.

References

1. G. Maccari, D. J. Barker, X. Georgiou, et al., "The IPD-IMGT/HLA Database," *Nucleic Acids Research* 51 (2023): D1053–D1060.

2. S. G. E. Marsh, E. D. Albert, W. F. Bodmer, et al., "Nomenclature for Factors of the HLA System, 2010," *Tissue Antigens* 75 (2010): 291–455.