

Characterization of the novel *HLA-DRB3*02:179N* allele by sequencing-based typing

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*HLA-DRB3*02:179N* differs from *DRB3*02:02:01:02* by one nucleotide substitution in codon 98 in exon 3.

KEYWORDS

HLA, *HLA-DRB3*02:179N*, novel allele, sequencing-based typing

We report here a novel *HLA-DRB3*02* allele, now named *DRB3*02:179N* that carries one nucleotide substitution in exon 4 when compared with the *DRB3*02:02:01:02* allele, identified in a volunteer bone marrow donor. The HLA typing was performed using Next Generation Sequencing (AllType NGS, One Lambda, Canoga Park, CA) on the Ion S5 system platform (ThermoFisher Scientific, Waltham, MA),¹ from exons 2 to 5. The reads were analyzed using the TypeStream Visual Software version 2.1 (One Lambda). This donor was found to have a new *DRB3*02* allele and was consequently typed *A*02:01*, *03:01*; *C*01:02*, *07:02*; *B*07:02*, *55:01*; *DRB1*11:01*, *11:03*; *DRB3*02:02*, *02:179N*; *DQA1*05:05*, *05:05*; *DQB1*03:01P*, *03:01P*; *DPA1*01:03*, *01:03*; *DPB1*04:01*, *04:02*. Using the IPD-IMGT/HLA Database,² nucleotide sequence alignment with HLA-DRB3 alleles shows that this new allele has one nucleotide change from *DRB3*02:02:01:02* in codon 98 in exon 3, where C → T resulting in a new

protein (CAG → TAG, Glutamine → STOP, Figure 1). This nucleotide change was confirmed by performing the typing twice in two different laboratories. We were confident in the phasing as the sample displayed a mean read length of 908 base pairs over all the loci, the mismatched T base was attributed 336 times to the new *HLA-DRB3*02* allele. As a null allele, the *HLA-DRB3*02:179N* is clinically significant in both organ and allogeneic hematopoietic cell transplantation. The coding nucleotide sequence of the new allele has been submitted to the GenBank database (Accession No. ON176159) and to the IPD-IMGT/HLA Database (Submission No. HWS10061074). The name *DRB3*02:179N* has been officially assigned by the WHO Nomenclature Committee for Factors of the HLA System in April 2022. This follows the agreed policy that, subject to the conditions stated in the most recent Nomenclature Report,³ names will be assigned to new sequences as they are identified. Lists of

AA Codon		100		105		110		115																		
DRB3*02:02:01:02	TC	CAT	CCT	CAG	GTG	ACT	GTG	TAT	CCT	GCA	AAG	ACC	CAG	CCC	CTG	CAG	CAC	CAC	AAC	CTC	CTG	GTC	TGC	TCT	GTG	
DRB3*02:179N	--	--	--	T--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	
AA Codon	120		125		130		135		140																	
DRB3*02:02:01:02	AGT	GGT	TTC	TAT	CCA	GGC	AGC	ATT	GAA	GTC	AGG	TGG	TTC	CGG	AAC	GGC	CAG	GAA	GAG	AAG	GCT	GGG	GTG	GTG	TCC	
DRB3*02:179N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
AA Codon	145		150		155		160		165																	
DRB3*02:02:01:02	ACG	GGC	CTG	ATC	CAG	AAT	GGA	GAC	TGG	ACC	TTC	CAG	ACC	CTG	GTG	ATG	CTA	GAA	ACA	GTT	CCT	CGG	AGT	GGA	GAG	
DRB3*02:179N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
AA Codon	170		175		180		185																			
DRB3*02:02:01:02	GTT	TAC	ACC	TGC	CAA	GTG	GAG	CAC	CCA	AGC	GTA	ACG	AGC	CCT	CTC	ACA	GTG	GAA	TGG	A						
DRB3*02:179N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---					

FIGURE 1 Alignment of the sequence of exon 3 of *HLA-DRB3*02:179N* with the sequence of *HLA-DRB3*02:02:01:02*. Dashes indicate nucleotide identity with the *HLA-DRB3*02:02:01:02* allele. Numbers above the sequence indicate codon position.

such new names will be published in the following WHO Nomenclature Report.

AUTHOR CONTRIBUTIONS

Marine Cargou and Jonathan Visentin contributed to the design of the study. Marine Cargou and Jonathan Visentin participated in the writing of the paper. Marine Cargou, Marco Andreani, Tiziana Galluccio, Lucie Blandin, and Jonathan Visentin participated in the performance of the research. Marine Cargou, Marco Andreani, Tiziana Galluccio, Lucie Blandin, and Jonathan Visentin participated in data analysis. Marco Andreani, Tiziana Galluccio, and Lucie Blandin were involved in critical revision of the manuscript.

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CONFLICT OF INTEREST

The authors confirm that there are no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or

ethical restrictions. The sequence is freely available in the IPD-IMGT/HLA Database.

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Identification of the novel *HLA-DRB4*01:162N* allele using next-generation sequencing

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The *HLA-DRB4*01:162N* allele differs from *HLA-DRB4*01:03:01:01* allele by a single nucleotide in codon 131.

KEYWORDS

HLA, *HLA-DRB4*01:162N*, new allele, next-generation sequencing