

HLA-C*05:292N, a novel HLA-C null allele identified by next-generation sequencing

Justine Schmitt  | André Gothot

HLA Typing Laboratory, Liège University Hospital, Liège, Belgium

Correspondence

Justine Schmitt, HLA Typing Laboratory, Liège University Hospital, Avenue de l'hôpital, 1, 4000 Liège, Belgium.
Email: justine.schmitt@chuliege.be

*HLA-C*05:292N* differs from *HLA-C*05:01:01:08* by a frameshift mutation, a deletion at gDNA position 758.

KEYWORDS

HLA-C, next generation sequencing, null allele

Identifying a null allele is important in hematopoietic stem cell transplantation to avoid a donor-recipient mismatch that could trigger T cell-driven host versus graft or graft versus host disease.¹ We describe here a novel null HLA-C allele, now named *C*05:292N*, that was identified in a Belgian hematopoietic stem cell recipient. The patient was diagnosed with acute myeloid leukemia in August 2023. 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 analyzed by NGSengine software and compared with the IPD/IMGT-HLA Database.² The sequencing data showed a best match to the *C*05:99N* allele although differing by 6 exon mismatches. When aligning this data with the closest related allele *C*05:01:01:08*, a mismatch in exon 3 was detected. A deletion at gDNA position 758 was exclusively present in the reads assigned to the *C*05* allele and not in the *C*03:04* allele also present in the patient. This deletion caused a frameshift with a resulting premature stop codon (TGA) in codon 126 (Figure 1).

To exclude the possibility that this null allele was derived from blast cells of the malignant clone,³ another sample was collected using a buccal swab and processed using the same NGS protocol. The deletion in exon 3 of the *C*05:292N* allele was confirmed. This information will indeed be taken into account for the patient to provide the best HLA-matched available donor. The complete HLA typing of the patient with this novel allele was: *HLA-A*02:01, 02:20; -B*40:01, 44:02; -C*03:04, 05:292N; -DRB1*13:02, 14:54;*

*-DRB3*02:02, 03:01; -DQB1*05:03, 06:04; -DQA1*01:02, 01:04; -DPA1*01:03; -DPB1*03:01, 04:01.*

The nucleotide sequence of the novel *HLA-C*05:292N* allele has been submitted to the GenBank database (accession number OR513911) and IPD-IMGT/HLA Database (submission ID HWS10067655). The name *C*05:292N* has been officially assigned by the WHO nomenclature Committee for Factors of the HLA system in November 2023.⁴ This follows the agreed policy that, subject to the conditions stated in the most recent Nomenclature Report, 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.

ACKNOWLEDGMENTS

The authors thank the HLA laboratory technicians of the University Hospital of Liège for their expertise.

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 openly available in IPD-IMGT/HLA Database at <https://www.ebi.ac.uk/ipd/hla/>, reference number HWS10067655.

AA Codon		80		85		90		95		100															
C*05:01:01:08	AAC	CTG	CGG	AAA	CTG	CGC	GGC	TAC	TAC	AAC	CAG	AGC	GAG	GCC	G GG	TCT	CAC	ACC	CTC	CAG	AGG	ATG	TAT	GCC	TGC
C*05:99N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	-	---	---	---	---	---	---	---	---	---	---
C*05:292N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	-	---	---	---	---	---	---	---	---	---	---
AA Codon		105		110		115		120		125															
C*05:01:01:08	GAC	CTG	GGG	CCC	GAC	GGG	CGC	CTC	CTC	CGC	GGG	TAT	AAC	CAG	TTC	GCC	TAC	GAC	GGC	AAG	GAT	TAC	ATC	GCC	CTG
C*05:99N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
C*05:292N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
AA Codon		130		135		140		145		150															
C*05:01:01:08	AAT	GAG	GAC	CTG	CGC	TCC	TGG	ACC	GCC	GCG	GAC	AAG	GCG	GCT	CAG	ATC	ACC	CAG	CGC	AAG	TGG	GAG	GCG	GCC	CGT
C*05:99N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
C*05:292N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
AA Codon		155		160		165		170		175															
C*05:01:01:08	GAG	GCG	GAG	CAG	CGG	AGA	GCC	TAC	CTG	GAG	GGC	ACG	TGC	GTG	GAG	TGG	CTC	CGC	AGA	TAC	CTG	GAG	AAC	GGG	AAG
C*05:99N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
C*05:292N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
AA Codon		180		185		190		195		200															
C*05:01:01:08	AAG	ACG	CTG	CAG	CGC	G AA	CAC	CCA	AAG	ACA	CAC	GTG	ACC	CAC	CAT	CCC	GTC	TCT	GAC	CAT	GAG	GCC	ACC	CTG	
C*05:99N	---	---	---	---	---	---	-	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
C*05:292N	---	---	---	---	---	---	-	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
AA Codon		205		210		215		220		225															
C*05:01:01:08	AGG	TGC	TGG	GCC	CTG	GGC	TTC	TAC	CCT	GCG	GAG	ATC	ACA	CTG	ACC	TGG	CAG	CGG	GAT	GGC	GAG	GAC	CAA	ACT	CAG
C*05:99N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
C*05:292N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
AA Codon		230		235		240		245		250															
C*05:01:01:08	GAC	ACC	GAG	CTT	GTG	GAG	ACC	AGG	CCA	GCA	GGA	GAT	GGA	ACC	TTC	CAG	AAG	TGG	GCA	GCT	GTG	GTG	GTG	CCT	TCT
C*05:99N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
C*05:292N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
AA Codon		255		260		265		270		275															
C*05:01:01:08	GGA	GAA	GAG	CAG	AGA	TAC	ACG	TGC	CAT	GTG	CAG	CAC	GAG	GGG	CTG	CCA	GAG	CCC	CTC	ACC	CTG	AGA	TGG	G GG	CCA
C*05:99N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	- A-
C*05:292N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	-
AA Codon		280		285		290		295		300															
C*05:01:01:08	TCT	TCC	CAG	CCC	ACC	ATC	CCC	ATC	GTG	GGC	ATC	GTT	GCT	GGC	CTG	GCT	GTC	CTG	GCT	GTC	CTA	GCT	GTC	CTA	GGA
C*05:99N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
C*05:292N	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---

FIGURE 1 Sequence alignment of exon 3 of the C*05:292N with the closely related HLA-C*05:01:01:08 allele. Dashes indicate nucleotide identity with the HLA-C*05:01:01:08 allele. Numbers above the sequence indicate codon position. The deletion of a single G nucleotide is indicated in position 104. The resulting TGA stop codon is located in codon 126.

ORCID

Justine Schmitt  <https://orcid.org/0009-0009-4900-0937>

REFERENCES

- Elsner HA, Blasczyk R. Immunogenetics of HLA null alleles: implications for blood stem cell transplantation. *Tissue Antigens*. 2004;64(6):687-695. doi:10.1111/j.1399-0039.2004.00322.x
- Barker DJ, Maccari G, Georgiou X, et al. The IPD/IMGT-HLA database. *Nucleic Acids Res*. 2023;51(D1):D1053-D1060. doi:10.1093/nar/gkac1011
- Arnold PY. Review: HLA loss and detection in the setting of relapse from HLA-mismatched hematopoietic cell transplant.

Hum Immunol. 2022;83(10):712-720. doi:10.1016/j.humimm.2022.03.001

- Marsh SGE, Albert ED, Bodmer WF, et al. Nomenclature for factors of the HLA system, 2010. *Tissue Antigens*. 2010;75:291-455.

How to cite this article: Schmitt J, Gothot A. HLA-C*05:292N, a novel HLA-C null allele identified by next-generation sequencing. *HLA*. 2024;103(2):e15380. doi:10.1111/tan.15380