Characterization of the novel *HLA-A*11:422* allele by sequencing-based typing

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*HLA-A*11:422* differs from *HLA-A*11:01:01:01* by one nucleotide substitution in codon 285 in exon 5.

KEYWORDS
HLA, *HLA-A*11:422*, novel allele, sequencing-based typing

We report here a novel *HLA-A*11* allele, now named *A*11:422*, that carries one nucleotide substitution in exon 5 when compared with the *A*11:01:01:01* 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 1 to 8. The reads were analyzed using the TypeStream Visual Software version 2.1 (One Lambda). This recipient was found to have a new *A*11* allele and was consequently typed *A*11:422, 30:02*; *C*05:01, 15:02*; *B*18:01, 51:01*; *DRB1*03:01, 13:02*; *DRB3*02:02, 03:01*; *DQA1*01:02, 05:01*; *DQB1*02:01, 06:04*; *DPA1*01:03, 01:03*; *DPB1*02:02, 04:01*. Using the IPD-IMGT/HLA Database,[2] nucleotide sequence alignment with HLA-A alleles shows that this new allele has one nucleotide change from *A*11:01:01:01* in codon 285 in exon 5, where G → A resulting in a new protein (GTG → ATG, Valine → Methionine, Figure 1). This nucleotide change was confirmed using other NGS reagents provided by Immucor (Mia Fora NGS Flex, Norcross, GA) run on the Illumina MiSeq system (San Diego, CA) and analyzed with the Mia Fora Flex software (Immucor, version 5.1). We were confident in the phasing as the sample displayed a mean read length of 427 base pairs over all the loci, the mismatched A base was attributed 310 times to the new *HLA-A*11* allele. HLA typing by Luminex reverse sequence-specific oligonucleotide (SSO) was performed (One Lambda Labtype XR, Canoga Park, CA).[3] With this assay (lot 004, catalog RSSOX1A_004_04), the HLA-typing of the patient was *HLA-A*11:DXFNW, 30:DXAVD* (most likely alleles *A*11:01, 30:02*) without any bead modification. Indeed, the IPD-IMGT/HLA Database 3.48.0 release shows that there are few other HLA-A alleles displaying a ATG sequence in codon 285, explaining why the manufacturer

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AA Codon                          280                 285                 290                 295
A*11:01:01:01       AG CTG TCT TCC CAG CCC ACC ATC CCC ATC GTG GGC ATC ATT GCT GGC CTG GTT CTC CTT GGA GCT GTG ATC ACT
A*11:422            -- --- --- --- --- --- --- --- --- --- A-- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon            300                 305                 310
A*11:01:01:01       GGA GCT GTG GTC GCT GCC GTG ATG TGG AGG AGG AAG AGC TCA G
A*11:422            --- --- --- --- --- --- --- --- --- --- --- --- --- --- -
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FIGURE 1 Alignment of the sequence of exon 5 of *A*11:422* with the sequence of *A*11:01:01:01*. Dashes indicate nucleotide identity with the *HLA-A*11:01:01:01* allele. Numbers above the sequence indicate codon position

did not include probes recognizing this allele. The analysis of the localization of this amino-acid and its antibody accessibility indicated it is not surface accessible and not located close to the peptide binding groove. Indeed, it is localized in the transmembrane region. Then, its clinical significance seems minimal. The coding nucleotide sequence of the new allele has been submitted to the GenBank database (Accession No. ON135542) and to the IPD-IMGT/HLA Database (Submission No. HWS10061020). The name *A*11:422* 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,[4] 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

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, Vincent Elsermans, Isabelle Top, Lucie Blandin, and Jonathan Visentin participated in the performance of the research. Marine Cargou, Vincent Elsermans, Isabelle Top, Lucie Blandin, and Jonathan Visentin participated in data analysis. Vincent Elsermans, Isabelle Top, and Lucie Blandin were involved in critical revision of the manuscript.

ACKNOWLEDGMENT

The authors thank the technicians of the Bordeaux and Lille Immunology laboratories for their technical expertise.

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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How to cite this article: Cargou M, Elsermans V, Top I, Blandin L, Visentin J. Characterization of the novel *HLA-A*11:422* allele by sequencing-based typing. *HLA*. 2022;100(6):624-625. doi:10.1111/tan.14757