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NEW ALLELE ALERT

The *HLA-A* Allele, *HLA-A*11:01:01:07*, Identified by Third-Generation Sequencing

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Received: 25 October 2024 | **Revised:** 4 November 2024 | **Accepted:** 7 November 2024

Funding: This work was supported by National Key R&D Program of China (grant no. 2022YFC2502700), Integrated Basic and Clinical Project of the First Affiliated Hospital of Xi'an Jiaotong University (grant no. YXJLRH2022007).

Keywords: *HLA-A*11:01:01:07* | novel allele | third-generation sequencing

ABSTRACT

*HLA-A*11:01:01:07* differs from *HLA-A*11:01:01:01* by a single nucleotide exchange in intron 1.

With the increased utilisation of new technologies, such as next-generation sequencing (NGS), for the routine practice of HLA typing, an increasing number of novel HLA alleles have been identified and deposited in the IPD-IMGT/HLA Database [1]. Herein, we report a confirmatory sequence of the *HLA-A*11:01:01:07* allele identified from a healthy female participant during a cohort investigation in Shaanxi Province, China. The complete HLA genotyping obtained for this individual was *HLA-A*11:01:01:07, 32:01:01; -B*15:12:01, 52:01:01; -C*12:02:02, 03:03:01; -DRB1*12:01:01, 15:02:01; -DRB3*01:01:02; -DRB5*01:02:01; -DQA1*01:03:01, 05:08; -DQB1*06:01:01, 03:01:01; -DPA1*02:02:02, 02:02:02; -DPB1*02:01:02, 05:01:01*.

High molecular weight (HMW) genomic DNA was extracted from peripheral blood mononuclear cells using the Monarch HMW DNA Extraction Kit for Cell & Blood (NEB, T3050L) in accordance with the manufacturer's manual. Multiplex PCR was applied to amplify each subject's HLA genes (*HLA-A*, *-B*, *-C*, *-DRB1*, *-DRB3*, *-DRB4*, *-DRB5*, *-DQA1*, *-DQB1*, *-DPA1* and *-DPB1*) for HiFi library preparation. The resulting libraries from different subjects were pooled and sequenced using the third-generation sequencing platform Pacific Biosciences Sequel II. Genotypes of the HLA genes were determined using the IPD-IMGT/HLA Database (version 3.50.0) along with several software packages including pbmm2, CCS, lima and WhatsHap.

Nucleotide sequence alignments with *HLA-A* alleles from the IPD-IMGT/HLA Sequence Database showed that the intron 1 sequence of the *HLA-A*11:01:01:07* allele was close to *HLA-A*11:01:01:01*, except for 1 nucleotide change at nucleotide 399 where C>G (Figure 1).

The confirmatory nucleotide sequence of this allele has been submitted to the GenBank database (Accession No. PP986995) and to the IPD-IMGT/HLA Database (Submission No. HWS10091199). The name *A*11:01:01:07* has been officially assigned by the WHO Nomenclature Committee for Factors of the HLA System in July 2017, our confirmatory sequence was submitted in August 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.

https://doi.org/10.1111/tan.15771

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Intron 1
gDNA                      380        390        400        410        420
A*11:01:01:01         GTGAGTG CGGGGTCGGG AGGGAAACCG CCTCTGCGGG GAGAAGCAAG
A*11:01:01:07         ------- ---------- --------G- ---------- ----------


gDNA                      430        440        450        460        470
A*11:01:01:01      GGGCCCTCCT GGCGGGGGCG CAGGACCGGG GGAGCCGCGC CGGGAGGAGG
A*11:01:01:07      ---------- ---------- ---------- ---------- ----------


gDNA                      480        490
A*11:01:01:01      GTCGGGCAGG TCTCAGCCAC TGC
A*11:01:01:07      ---------- ---------- ---
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FIGURE 1 | Alignment of the of intron 1 sequence of *HLA-A*11:01:01:07* allele with the sequence of *HLA-A*11:01:01:01*. Dashes (–) indicate nucleotide identity with the *HLA-A*11:01:01:01* allele. Numbers above the sequence indicate the position.

Author Contributions

Yingjie Chen, Yuqi Wang and Huachao Zhu collected samples, analysed the data, submitted sequence data to GenBank and IPD-IMGT/HLA Database and wrote the manuscript. Yuqi Wang did the sequencing. Juan Ren reviewed the manuscript. Xiaoning Wang designed the study and reviewed the manuscript. All authors have read and approved the final manuscript.

Acknowledgements

The authors would like to offer sincere gratitude to the volunteer donors for participation in their bone marrow donor registry. This work was supported by National Key R&D Program of China (grant no. 2022YFC2502700) and Integrated Basic and Clinical Project of the First Affiliated Hospital of Xi'an Jiaotong University (grant no. YXJLRH2022007).

Conflicts of Interest

The authors declare 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.

References

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