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NEW ALLELE ALERT

Detection of the Novel *HLA-A*02:01:01:257* Allele by Pacific Biosciences HiFi Sequencing in a Chinese Individual

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ABSTRACT

*HLA-A*02:01:01:257* differs from *HLA-A*02:01:01:01* by a single nucleotide substitution in intron 7.

We describe here the identification of the novel *HLA-A*02* allele, now officially named *HLA-A*02:01:01:257*, exhibiting 1 nucleotide difference from *HLA-A*02:01:01:01* in intron 7 at nucleotide 2868 where C>G (Figure 1). This nucleotide alteration was revealed through our investigation involving a cohort of healthy Chinese individuals, with the specific variant identified in one female participant. The complete HLA genotyping obtained for this individual was: *HLA-A*02:01:01:257, 24:02:01; -B*40:06:01, 57:01:01; -C*06:02:01, 08:01:01; -DRB1*07:01:01, 12:01:01; -DRB3*01:01:02; -DRB4*01:03:01; -DQA1*02:01:01, 05:05:01; -DQB1*03:01:01, 03:03:02; -DPA1*02:02:02; -DPB1*05:01:01*.

High-molecular weight (HMW) genomic DNA was extracted from peripheral blood mononuclear cells (PBMCs) using the Monarch HMW DNA Extraction Kit for Cell & Blood (NEB, T3050L), in accordance with the manufacturer's instruction. Multiplex PCR was conducted to amplify all the 11 classical HLA genes of each subject, specifically *HLA-A*, *-B*, *-C*, *-DRB1*, *-DRB3*, *-DRB4*, *-DRB5*, *-DQA1*, *-DQB1*, *-DPA1* and *-DPB1*, for the preparation of HiFi libraries. The resulting libraries from different subjects were subsequently pooled and sequenced using the Pacific Biosciences Sequel II third-generation sequencing platform. The genotypes of the HLA genes were determined using the IPD-IMGT/HLA Database (version 3.57.0) along with several software packages including pbmm2, CCS, lima and WhatsHap.

The nucleotide sequence of the new allele has been submitted to the GenBank database (Accession number PQ212803) and to the IPD-IMGT/HLA Database (Submission number HWS10092155) [1]. The name *A*02:01:01:257* 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.

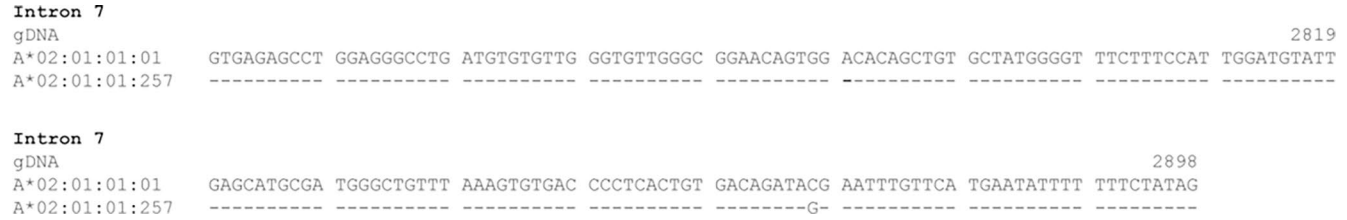

FIGURE 1 | Sequence alignment of *HLA-A* gene, intron 7 nucleotide sequences of the novel *HLA-A*02:01:01:257* allele and the closely related *HLA-A*02:01:01:01* allele. One single nucleotide substitution (C>G) was detected in intron 7 at position 2868. Dashes (-) indicate nucleotide identity between the two alleles. The numbers above the sequence indicate the *HLA-A*02:01:01:257* allele gDNA position.

Author Contributions

Yue Han, Yundie Liu, Caili Wang and Shaoqing Feng collected samples and analysed the data. Yue Han and Yundie Liu submitted the sequence data to GenBank and IPD-IMGT/HLA Database and wrote the manuscript. Yue Han did the sequencing. Peng Gao designed the study and reviewed the manuscript. All authors have read and approved the final manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Information of this study is freely available from the IPD-IMGT/HLA Database.

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