

NEW ALLELE ALERT

Identification of the Novel *HLA-DPA1*02:146* Allele by PacBio Sequencing

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ABSTRACT

The novel *HLA-DPA1*02:146* allele differs from *HLA-DPA1*02:20* by one nucleotide substitution in exon 2.

In this report, we describe the identification of the novel allele *HLA-DPA1*02:146*, which was identified by PacBio's Single Molecule Real-Time (SMRT) sequencing (PacBio, Menlo Park, CA, USA) of a sample from a Chinese haematopoietic stem cell donor.

Genomic DNA was isolated from a peripheral blood sample using commercial kits (Tiangen Biochemical Technology Co. Ltd., Beijing, China). Full-length gene segments of *HLA-A*, *HLA-B*, *HLA-C*, *HLA-DQB1*, *HLA-DPB1*, *HLA-DQA1* and *HLA-DPA1* were amplified with locus-specific primers. Additionally, the *DRB1*/3/4/5 genes were targeted using two primer pairs to amplify exon 1 and exons 2–6 individually. Next, SMRT sequencing of the amplicons was carried out using the PacBio Sequel II Platform, while readings were analysed by PB AMPLICON ANALYSIS (PBAA) software (Version 1.0.3).

The complete HLA typing of the 34-year-old patient was as follows: *A*11:01, 24:02; B*15:02, 40:06; C*03:04, 08:01; DRB1*04:05, 15:01; DRB4*01:03; DRB5*01:01; DQA1*01:02, 03:03; DQB1*04:01, 06:01; DPA1*02:146, 04:01; DPB1*05:01, 107:01*.

Using *HLA-DPA1*02:20* sequence alignment from the IPD-IMGT/HLA 3.58 database [1], it was clear that the investigated allele differed from the allele *DPA1*02:20* at nucleotide 344 located in exon 2. The observed nucleotide substitution produced a non-synonymous variation from G to T at nucleotide 344, in codon 84 (AGT vs. ATT) resulting in a change from Serine to Isoleucine (Figure 1), indicating the existence of a new allele.

The sequence of the *DPA1*02:146* allele was submitted to Sequence Read Archive (SRA) and IPD-IMGT/HLA Database (the accession numbers are SUB14663781 and HWS10092011, respectively).

The name *HLA-DPA1*02:146* was officially assigned by the WHO Nomenclature Committee for Factors of the HLA System in September 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.

Bin Chen and Tongcui An contributed equally to this study.

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|-------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| AA Codon | | 5 | | 10 | | 15 | | 20 | | 25 | | | | | | | | | | | | | | | | |
| DPA1*02:20 | CG | GAC | CAT | GTG | TCA | ACT | TAT | GCC | ATG | TTT | GTA | CAG | ACC | CAT | AGA | CCA | ACA | GGA | GAG | TTT | ATG | TTT | GAA | TTT | GAT | |
| DPA1*02:146 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | |
| AA Codon | | 30 | | 35 | | 40 | | 45 | | 50 | | | | | | | | | | | | | | | | |
| DPA1*02:20 | GAA | GAT | GAG | CAG | TTC | TAT | GTG | GAT | CTG | GAC | AAG | AAG | GAG | ACC | GTC | TGG | CAT | CTG | GAG | GAG | TTT | GGC | CGA | GCC | TTT | |
| DPA1*02:146 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | |
| AA Codon | | 55 | | 60 | | 65 | | 70 | | 75 | | | | | | | | | | | | | | | | |
| DPA1*02:20 | TCC | TTT | GAG | GCT | CAG | GGC | GGG | CTG | GCT | AAC | ATT | GCT | ATA | TTG | AAC | AAC | AAC | TTG | AAT | ACC | TTG | ATC | CAG | CGT | TCC | |
| DPA1*02:146 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | |
| AA Codon | | 80 | | | | | | | | | | | | | | | | | | | | | | | | |
| DPA1*02:20 | AAC | CAC | ACT | CAG | GCC | GCC | AGT | G | | | | | | | | | | | | | | | | | | |
| DPA1*02:146 | -- | -- | -- | -- | -- | -- | -T- | - | | | | | | | | | | | | | | | | | | |

FIGURE 1 | Comparison of the exon 2 sequences of the *HLA-DPA1*02:20* and *HLA-DPA1*02:146* alleles. The exon 2 sequences are shown in codons, numbered above. One nucleotide substitution in codon 84 present in *HLA-DPA1*02:146* distinguishes it from the *HLA-DPA1*02:20* allele. Identity between the two sequences is shown with dashes (-).

Author Contributions

Kun Ru and Chengping Li designed the study. Tongcui An provided genetic laboratory data. Bin Chen and Yani Lin analysed the data and wrote the manuscript. All authors read and approved the final version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data have been submitted to both [Sequence Read Archive \(SRA\)](#) and IPD-IMGT/HLA Database (the accession numbers are SUB14663781 and HWS10092011, respectively).

References

1. J. Robinson, D. J. Barker, and S. G. E. Marsh, "25 Years of the IPD-IMGT/HLA Database," *HLA* 103, no. 6 (2024): e15549.
2. S. G. E. Marsh, E. D. Albert, W. F. Bodmer, et al., "Nomenclature for Factors of the HLA System, 2010," *Tissue Antigens* 75, no. 4 (2010): 291–455.