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NEW ALLELE ALERT

HLA Immune Response Genetics WILEY

Identification of the novel *HLA-A*11:456* allele by next-generation sequencing

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*HLA-A*11:456* has one non-synonymous nucleotide substitution compared to *HLA-A*11:02:01:01* at position 565 in exon 3.

KEYWORDS
HLA, *A*11:456*, new allele

The HLA system is located within the human major histocompatibility complex (MHC) on the short arm of chromosome 6, the HLA genes are the most polymorphic in the human genome,[1] and play a central role in the immune response.[2] To date, 36,814 alleles have been identified according to the IPD-IMGT/HLA Database Release 3.53 version.[3] Here, we report a novel allele *HLA-A*11:456* comes from a Chinese bone marrow donor, which differs from *HLA-A*11:02:01:01* by one nucleotide substitution.

The sample was originally genotyped for *HLA-A, -B,-C,-DRB1* and *-DQB1* by polymerase chain reaction-sequence specific oligonucleotide(PCR-SSO) method with LABType XR DNA Typing Kit and analyzed with HLA Fusion software V4.6 (One Lambda, Inc., West Hills, CA, USA). The sequencing results of *HLA-A* in

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                91                                                                  110
A*11:02:01:01   GT TCT CAC ACC ATC CAG ATA ATG TAT GGC TGC GAC GTG GGG CCG GAC GGG CGC TTC CTC

A*11:456        -- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

               111                                                                  130
A*11:02:01:01   CGC GGG TAC CGG CAG GAC GCC TAC GAC GGC AAG GAT TAC ATC GCC CTG AAC GAG GAC CTG

A*11:456        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

               131                                                                  150
A*11:02:01:01   CGC TCT TGG ACC GCG GCG GAC ATG GCA GCT CAG ATC ACC AAG CGC AAG TGG GAG GCG GCC

A*11:456        --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

               151                                                                  170
A*11:02:01:01   CAT GCG GCG GAG CAG CAG AGA GCC TAC CTG GAG GGC CGG TGC GTG GAG TGG CTC CGC AGA

A*11:456        --- --- --- --- --- --- --- --- --- --- --- --- --- --- T-- --- --- --- --- ---

               171                                                 183
A*11:02:01:01   TAC CTG GAG AAC GGG AAG GAG ACG CTG CAG CGC ACG G

A*11:456        --- --- --- --- --- --- --- --- --- --- --- --- -
```

FIGURE 1 Alignment of the exon 3 of *HLA-A*11:456 with the sequence of HLA-A*11:02:01:01*. Dashes indicate nucleotide identity with the *HLA-A*11:02:01:01*sequence. Numbers above the sequence correspond to the codon position.

the sample did not fully match any allele combination. In order to identify it, polymerase chain reaction sequence-based typing (TBG Biotechnology Corp., Xiamen，China) was used. we amplified the *HLA-A*02 and HLA-A*11* separately with group specific primers. The sequence reaction products were processed with an ABI 3130XL DNA Analyzer (Applied Biosystems, Foster City, USA) and analyzed with AccuType software V1.5(TBG Biotechnology Corp., Xiamen，China). The sequencing results showed that the *HLA- A* alleles of the donor were *HLA-A*02:01* and a novel allele, now named *HLA-A*11:456*. Meanwhile, the sample was also genotyped by next-generation sequencing method with AllType 11-Loci Amplification Kit (One Lambda, Inc., Canoga Park, USA). The sequence reaction products were processed with an Ion GeneStudio S5 plus Sequencing Analyzer (Thermo Fisher Scientific, Waltham, MA, USA) and analyzed with TypeStream Visual NGS Analysis Software 3.0 (One Lambda, Inc., West Hills, CA, USA). Compared with the *HLA-A*11:02:01:01*, the novel *HLA-A*11:456* shows one nucleotide substitution from G to T at position 565 (Codon 91) in exon 3 which resulting in a coding change from Valine to Leucine at residue 165 (Figure 1). The nucleotide sequence has been submitted to the GenBank nucleotide sequence database and assigned the accession number OR513024. The complete HLA genotype of the donor was *HLA-A*02:01, 11:456; -B*13:01, 40:01; -C*03:04, 03:04; -DRB1*08:02, 11:01*; *-DQB1*03:01, 04:02*.

The name *HLA-A*11:456* has been officially assigned by the WHO Nomenclature Committee for Factors of the HLA System in September 2023. 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

Jianbin Li conceived the project. Zheng Liu designed, supervised the experiments and wrote the manuscript. Yiqing Kang, Ziqing Wang and Yamin Sun performed the experiments and analyzed the data.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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