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NEW ALLELE ALERTS

HLA Immune Response Genetics WILEY

Discovery of a novel HLA class I allele, *HLA-B*38:75*, in an Indian umbilical cord blood sample

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The novel HLA allele *HLA-B*38:75* differs from *B*38:02:01* by nonsynonymous change in codon 50.

KEYWORDS
cord blood units, human leukocyte antigen, next generation sequencing

The HLA genes, located within the human major histocompatibility complex on the short-arm chromosome 6 (6p21.3), are known for their extreme polymorphism and encode the diverse HLA class I and II antigen-presenting molecules. According to the IPD-IMGT/HLA Database, the HLA-B gene is most polymorphic encoding over 6500 alleles (Release 3.27.0 July 2019).[1] The number of HLA alleles recognized is continuously increasing with the development of genotyping technologies.

We discovered the novel HLA-B allele during routine HLA typing of samples derived from umbilical cord blood by next generation sequencing (NGS) method. In comparison to traditional HLA DNA typing methods, the NGS technique has several advantages: first, it allows generation of haplotype sequencing from a single DNA molecule; second, it resolves the problem of phase ambiguity and last, millions of sequencing reads are produced by massive level of parallelism. As such, NGS is expected to

Segment :Exon2

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AA Codon                    5                   10                  15                  20
B*38:02:01      GC  TCC CAC TCC ATG AGG TAT TTC TAC ACC TCC GTG TCC CGG CCC GGC CGC GGG GAG CCC
B*38:75         --  --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon                    25                  30                  35                  40
B*38:02:01      CGC TTC ATC TCA GTG GGC TAC GTG GAC GAC ACG CAG TTC GTG AGG TTC GAC AGC GAC GCC
B*38:75         --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon                    45                  50                  55                  60
B*38:02:01      GCG AGT CCG AGA GAG GAG CCG CGG GCG CCG TGG ATA GAG CAG GAG GGG CCG GAA TAT TGG
B*38:75         --- --- --- --- --- --- --- --- --- -T- --- --- --- --- --- --- --- --- --- ---

AA Codon                    65                  70                  75                  80
B*38:02:01      GAC CGG AAC ACA CAG ATC TGC AAG ACC AAC ACA CAG ACT TAC CGA GAG AAC CTG CGC ACC
B*38:75         --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

AA Codon                    85                  90
B*38:02:01      GCG CTC CGC TAC TAC AAC CAG AGC GAG GCC G
B*38:75         --- --- --- --- --- --- --- --- --- --- -
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FIGURE 1 Alignment of the exon 2 sequences of *HLA-B*38:02:01* with the new variant *B*38:75*. Dashes indicate nucleotide sequence identity to *B*38:02:01*. Numbers above correspond with the codon position

provide highly accurate, reproducible, more effective, and high-throughput genotyping of HLA gene.[2]

Briefly, DNA was extracted from whole blood using FABG reagent (Favorprep, Genomic DNA Mini Kit, Taiwan). The concentration of the extracted nucleic acid was measured using a Qubit dsDNA BR Assay Kit (Thermo Fisher Scientific). DNA concentration of 10 ng/μL was used for HLA sequencing and typing testing by using Illumina MiSeq/HiSeq, and analysis of data was done using in-house software (Histo S).

Point mutation, recombination, and gene conversion—such events have all been shown in the generation of novel HLA alleles. HLA polymorphism is mainly located in the exons that encode the α1 and α2 (HLA class I, exons 2-3) and the α1 and β1 (HLA class II, exon 2) domains which bind processed peptides.[3] In our HLA registry, we discovered the novel allele, now named *HLA-B*38:75*, which differs from the *HLA-B*38:02:01* allele by a nonsynonymous substitution (CCG to CTG, proline to leucine) in codon 50 in exon 2 (Figure 1).

The nucleotide sequence described in this study has been submitted to the GenBank and was allotted the accession number MG756820. The name *B*38:75* has been officially assigned by the World Health Organization (WHO) Nomenclature Committee in September 2018. 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.

CONFLICT OF INTEREST

The authors have declared no conflicting interests.

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REFERENCES

1. Robinson J, Halliwell JA, Hayhurst JD, Flicek P, Parham P, Marsh SG. The IPD and IMGT/HLA database: allele variant databases. *Nucleic Acids Res*. 2015;43:D423-D431.
2. Gandhi MJ, Ferriola D, Huang Y, Duke JL, Monos D. Targeted next-generation sequencing for human leukocyte antigen typing in a clinical laboratory: metrics of relevance and considerations for its successful implementation. *Arch Pathol Lab Med*. 2017;141(6):806-812.
3. Little AM, Parham P. Polymorphism and evolution of HLA class I and II genes and molecules. *Rev Immunogenet*. 1999;1(1):105-123.
4. Marsh SGE, Albert ED, Bodmer WF, et al. Nomenclature for factors of the HLA system, 2010. *Tissue Antigens*. 2010;75:291-455.

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