TISSUE ANTIGENS
IMMUNE RESPONSE GENETICS

A novel HLA-A allele, *A*74:23*, identified in an individual from Costa Rica

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The new *HLA-A*74:23* allele differs from the closest allele *A*74:01* by a nucleotide change in exon 3 at codon 97.

The human leucocyte antigen (HLA) system is the most polymorphic in the human genome. The current release of the IMGT/HLA Database (release 3.17.0 August 2014) includes over 11,800 HLA alleles, with 2884 alleles of the HLA-A gene (1). In this report, we present a novel HLA-A allele, *A*74:23*, identified in a sample from a Hispanic subject from the province of Guanacaste in Costa Rica. This population study sample was typed for HLA loci A, B, C and DRB1 using an in-house sequence-based typing (SBT) protocol aimed at exons 2, 3 and 4 for HLA-A, -B and -C, and exon 2 for HLA-DRB1. Genomic DNA was extracted from whole blood, and SBT for the four HLA loci was carried out using the BigDye® Terminator v3.1 chemistry (Invitrogen Life Technologies, Carlsbad, CA) on an ABI PRISM® 3730xl Genetic Analyzer (Applied Biosystems, Carlsbad, CA). The sequences were analyzed with Assign SBT v3.6.1.33 (Conexio Genomics, Fremantle, Australia). The high-resolution HLA typing for this individual was *A*11:01:01*, *A*74:new*, *B*07:02:01*, *B*49:01:01*, *C*07:01:01*, *C*07:02:01*, *DRB1*01:01:01G*, *DRB1*15:03:01G*. Analysis of the generic HLA-A sequence and comparison to the consensus *A*11:01:01* and *A*74:01* sequences revealed that this sample carried an *A*74*-related single nucleotide polymorphism (SNP) at coding DNA sequence (CDS) position 363. This result was confirmed with a second generic amplification and sequencing.

In order to further confirm this novel allele, allele-specific amplification of the *A*74* variant was carried out using an in-house HLA-A group-specific protocol. Sequencing of this allele-specific amplification was carried out, and analysis of the sequence confirmed the presence of a SNP at the aforementioned position.

The mono-allelic sequencing result showed that this new HLA-A allele differs from the closest allele *A*74:01* by a nucleotide change in exon 3 at codon 97 (ATG to ATA), resulting in a coding change from methionine to isoleucine (Figure 1).

The coding sequence for exons 2, 3 and 4 was submitted to the European Molecular Biology Laboratory and the accession number LM651040 assigned. The sequence was also submitted to the IMGT/HLA Database, where the name *HLA-A*74:23* has been officially assigned by the WHO Nomenclature Committee in August 2014. 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.

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Codon                               5                  10                  15                  20                  25
A*01:01:01:01        GC TCC CAC TCC ATG AGG TAT TTC TTC ACA TCC GTG TCC CGG CCC GGC CGC GGG GAG CCC CGC TTC ATC GCC GTG
A*74:01              -- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
A*74:23              -- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

Codon                              30                  35                  40                  45                  50
A*01:01:01:01      GGC TAC GTG GAC GAC ACG CAG TTC GTG CGG TTC GAC AGC GAC GCC GCG AGC CAG AAG ATG GAG CCG CGG GCG CCG
A*74:01            --- --- --- --- --- --- --- --- --- --- --T --- --- --- --- --- --- --- -G- --- --- --- --- --- ---
A*74:23            --- --- --- --- --- --- --- --- --- --- --T --- --- --- --- --- --- --- -G- --- --- --- --- --- ---

Codon                              55                  60                  65                  70                  75
A*01:01:01:01      TGG ATA GAG CAG GAG GGG CCG GAG TAT TGG GAC CAG GAG ACA CGG AAT ATG AAG GCC CAC TCA CAG ACT GAC CGA
A*74:01            --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- G-- --- --- --- --- --- --- --- ---
A*74:23            --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- G-- --- --- --- --- --- --- --- ---

Codon                              80                  85                  90                   95                  100
A*01:01:01:01      GCG AAC CTG GGG ACC CTG CGC GGC TAC TAC AAC CAG AGC GAG GAC G|GT TCT CAC ACC ATC CAG ATA ATG TAT GGC
A*74:01            -T- G-- --- --- --- --- --- --- --- --- --- --- --- --- -C- -|-- --- --- --- --- --- --G --- --- ---
A*74:23            -T- G-- --- --- --- --- --- --- --- --- --- --- --- --- -C- -|-- --- --- --- --- --- --- --- --- ---

Codon                              105                 110                 115                 120                 125
A*01:01:01:01      TGC GAC GTG GGG CCG GAC GGG CGC TTC CTC CGC GGG TAC CGG CAG GAC GCC TAC GAC GGC AAG GAT TAC ATC GCC
A*74:01            --- --- --- --- --- --- --- --- C-- --- --- --- --- -A- --- --- --- --- --- --- --- --- --- --- ---
A*74:23            --- --- --- --- --- --- --- --- C-- --- --- --- --- -A- --- --- --- --- --- --- --- --- --- --- ---

Codon                              130                 135                 140                 145                 150
A*01:01:01:01      CTG AAC GAG GAC CTG CGC TCT TGG ACC GCG GCG GAC ATG GCA GCT CAG ATC ACC AAG CGC AAG TGG GAG GCG GTC
A*74:01            T-- --- --- --- --- --- --- --- --- --- --- --- --- --G --- --- --- --- C-- --- --- --- --- --- -C-
A*74:23            T-- --- --- --- --- --- --- --- --- --- --- --- --- --G --- --- --- --- C-- --- --- --- --- --- -C-

Codon                              155                 160                 165                 170                 175
A*01:01:01:01      CAT GCG GCG GAG CAG CGG AGA GTC TAC CTG GAG GGC CGG TGC GTG GAC GGG CTC CGC AGA TAC CTG GAG AAC GGG
A*74:01            -G- -T- --- --- --- TT- --- -C- --- --- --- --- AC- --- --- --G T-- --- --- --- --- --- --- --- ---
A*74:23            -G- -T- --- --- --- TT- --- -C- --- --- --- --- AC- --- --- --G T-- --- --- --- --- --- --- --- ---

Codon                              180                  185                 190                 195                 200
A*01:01:01:01      AAG GAG ACG CTG CAG CGC ACG G|AC CCC CCC AAG ACA CAT ATG ACC CAC CAC CCC ATC TCT GAC CAT GAG GCC ACC
A*74:01            --- --- --- --- --- --- --- -|-- G-- --- --- --G --- --- --T --- --- G-T G-- --- --- --- --- --- ---
A*74:23            --- --- --- --- --- --- --- -|-- G-- --- --- --G --- --- --T --- --- G-T G-- --- --- --- --- --- ---

Codon                              205                 210                 215                 220                 225
A*01:01:01:01      CTG AGG TGC TGG GCC CTG GGC TTC TAC CCT GCG GAG ATC ACA CTG ACC TGG CAG CGG GAT GGG GAG GAC CAG ACC
A*74:01            --- --- --- --- --- --- A-- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
A*74:23            --- --- --- --- --- --- A-- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---

Codon                              230                 235                 240                 245                 250
A*01:01:01:01      CAG GAC ACG GAG CTC GTG GAG ACC AGG CCT GCA GGG GAT GGA ACC TTC CAG AAG TGG GCG GCT GTG GTG GTG CCT
A*74:01            --- --- --- --- --T --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- T-- --- --- --- ---
A*74:23            --- --- --- --- --T --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- T-- --- --- --- ---

Codon                              255                 260                 265                 270
A*01:01:01:01      TCT GGA GAG GAG CAG AGA TAC ACC TGC CAT GTG CAG CAT GAG GGT CTG CCC AAG CCC CTC ACC CTG AGA TGG G
A*74:23            --- --- C-- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- -
A*74:01            --- --- C-- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- -!
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Figure 1 Alignment of the novel *HLA-A*74:23* allele. The *A*74:23* and closely related *A*74:01* allele sequences for exons 2, 3 and 4 are shown in comparison with the *A*01:01:01:01* reference allele. Identity to the reference allele is shown by hyphens (-), the exon boundaries are indicated by pipes (|). Numbering is as used in the IMGT/HLA Database (1).

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Conflict of interest

The authors have declared no conflicting interests.

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