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SPECIAL REPORT

An update to HLA Nomenclature, 2010

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The WHO Nomenclature Committee for Factors of the HLA System met during the 15th International Histocompatibility and Immunogenetics Workshop in Buzios, Brazil in September 2008. This update is an extract of the main report that documents the additions and revisions to the nomenclature of human leukocyte antigen (HLA) specificities following the principles established in previous reports.
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Introduction of colon-delimited HLA allele names

The convention of using a four-digit code to distinguish HLA alleles that differ in the proteins they encode was introduced in the 1987 Nomenclature Report.[1,2] Since then additional digits have been added, and currently an allele name may be composed of four, six or eight digits depending on its sequence.

The first two digits describe the allele family, which often corresponds to the serological antigen carried by the allotype. The third and fourth digits are assigned in the order in which the sequences have been determined. Alleles whose numbers differ in the first four digits must differ in one or more nucleotide substitutions that change the amino-acid sequence of the encoded protein. Alleles that differ only by synonymous nucleotide substitutions within the coding sequence are distinguished by the use of the fifth and sixth digits. Alleles that differ only by sequence polymorphisms in introns or in the 5′ and 3′ untranslated regions that flank the exons and introns are distinguished by the use of the seventh and eight digits.

In 2002 we faced the issue of the *A*02* and *B*15* allele families having more than 100 alleles.[3] At that time the decision taken was to name further alleles in these families in the rollover allele families *A*92* and *B*95*, respectively. For *HLA-DPB1* alleles, it was decided to assign new alleles within the existing system; hence, once *DPB1*9901* had been assigned the next allele would be assigned *DPB1*0102*, followed by *DPB1*0203*, *DPB1*0302* etc.

When these conventions were adopted, it was anticipated that the nomenclature system would accommodate all the HLA alleles likely to be sequenced. Unfortunately this is not the case, as the number of alleles for certain genes is now fast approaching the maximum possible with the current naming convention.

With the ever-increasing number of HLA alleles described, it has been decided to introduce colons (:) into the allele names to act as delimiters of the separate fields. To facilitate the transition from the old to the new nomenclature, a single leading zero must be added to all fields containing the values 1–9, but beyond that no leading zeros are allowed. This will help to lessen any confusion in the conversion to the new style of nomenclature.

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Hence:

*A*01010101*	becomes	*A*01:01:01:01*
*A*02010102L*	becomes	*A*02:01:01:02L*
*A*260101*	becomes	*A*26:01:01*
*A*3301*	becomes	*A*33:01*
*B*0808N*	becomes	*B*08:08N*
*DRB1*01010101*	becomes	*DRB1*01:01:01:01*

For allele families that have more than 100 alleles, such as the *A*02* and *B*15* groups, it will be possible to encode these in a single series. Thus, the *A*92* and *B*95* alleles will now be renamed into the *A*02* and *B*15* allele series. For example:

*A*9201*	becomes	*A*02:101*
*A*9202*	becomes	*A*02:102*
*A*9203*	becomes	*A*02:103* etc
*B*9501*	becomes	*B*15:101*
*B*9502*	becomes	*B*15:102*
*B*9503*	becomes	*B*15:103* etc

The names *A*02:100* and *B*15:100* will not be assigned. In case of other allele families in which the number of alleles reaches 100, these will be numbered sequentially; for example, *A*24:99* will be followed by *A*24:100*.

The *DPB1* allele names that have been previously assigned names within the existing system will also be renamed, for example:

*DPB1*0102*	becomes	*DPB1*100:01*
*DPB1*0203*	becomes	*DPB1*101:01*
*DPB1*0302*	becomes	*DPB1*102:01*
*DPB1*0403*	becomes	*DPB1*103:01*
*DPB1*0502*	becomes	*DPB1*104:01* etc

The 'w' will be removed from the *HLA-C* allele names, but will be retained in the HLA-C antigen names, to avoid confusion with the factors of the complement system and epitopes on the HLA-C molecule, often termed C1 and C2, that act as ligands for the killer-cell Ig-like receptors.

*Cw*0103*	becomes	*C*01:03*
*Cw*020201*	becomes	*C*02:02:01*
*Cw*07020101*	becomes	*C*07:02:01:01* etc

The changes to the HLA Nomenclature will be officially introduced in April 2010. A full list of old and new HLA allele names will be made available through the IMGT/HLA Database (www.ebi.ac.uk/imgt/hla) and the HLA Nomenclature web site (hla.alleles.org).[4]

Reporting of ambiguous HLA allele typing

The level of resolution achieved by many of the HLA typing technologies used today does not always allow for a single HLA allele to be unambiguously assigned. Often it is only possible to resolve the presence of a number of closely related alleles. This is referred to as an ambiguous 'string' of alleles. In addition, typing strategies are frequently aimed at resolving alleles that encode differences within the peptide-binding domains, but fail to exclude those that differ elsewhere. For some purposes it is helpful to provide codes that aid the reporting of certain ambiguous allele 'strings'. The decision was taken to introduce codes to allow for the easy reporting of the following:

(a) *HLA alleles that encode for identical peptide-binding domains*: HLA alleles having nucleotide sequences that encode the same protein sequence for the peptide-binding domains (exons 2 and 3 for HLA class I and exon 2 only for HLA class II alleles) will be designated by an upper case 'P', which follows the allele designation of the lowest-numbered allele in the group.

For example, the string of allele names below share the same α1 and α2 domain protein sequence encoded by exons 2 and 3:

*A*02:01:01:01/A*02:01:01:02L/A*02:01:01:03/*
*A*02:01:02/A*02:01:03/A*02:01:04/A*02:01:05/*
*A*02:01:06/A*02:01:07/A*02:01:08/A*02:01:09/*
*A*02:01:10/A*02:01:11/A*02:01:12/A*02:01:13/*
*A*02:01:14/A*02:01:15/A*02:01:17/A*02:01:18/*
*A*02:01:19/A*02:01:21/A*02:01:22/A*02:09/*
*A*02:66/A*02:75/A*02:89/A*02:97/A*02:132/*
*A*02:134/A*02:140*

This string can be reduced to *A*02:01P*.

(b) *HLA alleles that share identical nucleotide sequences for the exons encoding the peptide-binding domains*: HLA alleles that have identical nucleotide sequences for the exons encoding the peptide-binding domains (exons 2 and 3 for HLA class I and exon 2 only for HLA class II alleles) will be designated by an upper case 'G', which follows the allele designation of the lowest-numbered allele in the group.

For example, the string of allele names below have identical exon 2 and 3 nucleotide sequences:

*A*02:01:01:01/A*02:01:01:02L/A*02:01:01:03/*
*A*02:01:08/A*02:01:11/A*02:01:14/A*02:01:15/*
*A*02:01:21/A*02:09/A*02:43N/A*02:66/*
*A*02:75/A*02:83N/A*02:89/A*02:97/A*02:132/*
*A*02:134/A*02:140*

This string can be reduced to *A*02:01:01G*.

These reporting codes will be implemented in April 2010 and will be made available through the IMGT/HLA Database (www.ebi.ac.uk/imgt/hla) and the HLA Nomenclature web site (hla.alleles.org).[4]

A full list of all currently assigned HLA alleles and antigens, together with information on the changes documented here, is published in the WHO Nomenclature Committee for Factors of the HLA System, 2010.[1]

Conflict of interest

The authors declare no conflict of interest.

References

1 Marsh SGE, Albert ED, Bodmer WF, Bontrop RE, Dupont B, Erlich HA *et al*. Nomenclature for Factors of the HLA System, 2010. *Tissue Antigens* 2010; **75**: 291–455.
2 Bodmer WF, Albert E, Bodmer JG, Dupont B, Mach B, Mayr WR *et al*. Nomenclature for Factors of the HLA System, 1987. In: Dupont B (ed). *Immunobiology of HLA*. Springer-Verlag: New York, 1989, pp 72–79.
3 Marsh SGE, Albert ED, Bodmer WF, Bontrop RE, Dupont B, Erlich HA *et al*. Nomenclature for Factors of the HLA System, 2002. *Tissue Antigens* 2002; **60**: 407–464.
4 Robinson J, Malik A, Parham P, Bodmer JG, Marsh SGE. IMGT/HLA Database—sequence database for the human major histocompatibility complex. *Tissue Antigens* 2000; **55**: 280–287.