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Journal
HLA, 81(4)

ISSN
2059-2302

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Publication Date
2013-04-01

DOI
10.1111/tan.12093

Peer reviewed

Published in final edited form as:
Tissue Antigens. 2013 April ; 81(4): 194–203. doi:10.1111/tan.12093.

Common and Well-Documented HLA Alleles: 2012 Update to the CWD Catalogue

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Abstract

We have updated the catalogue of common and well-documented (CWD) HLA alleles to reflect current understanding of the prevalence of specific allele sequences. The original CWD catalogue designated 721 alleles at the HLA-A, -B, -C, -DRB1, -DRB3/4/5, -DQA1, -DQB1, and –DPB1 loci in IMGT/HLA Database release 2.15.0 as being CWD. The updated CWD catalogue designates 1122 alleles at the HLA-A, -B, -C, -DRB1, -DRB3/4/5, -DQA1, -DQB1, -DPA1 and –DPB1 loci as being CWD, and represents 14.3% of the HLA alleles in IMGT/HLA Database

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Conflicts of Interest
The authors have declared no conflicting interests.

release 3.9.0. In particular, we identified 415 of these alleles as being “common” (having known frequencies) and 707 as being “well-documented” on the basis of ~140,000 sequence-based typing observations and available HLA haplotype data. Using these allele prevalence data, we have also assigned CWD status to specific G and P designations. We identified 147/151 G groups and 290/415 P groups as being CWD. The CWD catalogue will be updated on a regular basis moving forward, and will incorporate changes to the IMGT/HLA Database as well as empirical data from the histocompatibility and immunogenetics community. This version 2.0.0 of the CWD catalogue is available online at cwd.immunogenomics.org, and will be integrated into the Allele Frequencies Net Database, the IMGT/HLA Database and National Marrow Donor Program’s bioinformatics web pages.

Keywords

allele prevalence; common allele; CWD; HLA; sequence based typing; well-documented allele

Introduction

The common and well-documented (CWD) catalogue was assembled by an American Society for Histocompatibility and Immunogenetics (ASHI) *ad-hoc* committee for the purpose of identifying alleles to be resolved in external proficiency testing (1). However, since its publication, the CWD catalogue has been used for a variety of applications that depend on a knowledge of allele prevalence (e.g., for the *in silico* reduction or resolution of genotyping ambiguity (2,3), as a criterion for studying specific alleles (4), and as an estimate of allele-frequency (5)), under the assumption that alleles not included in the CWD catalogue were unlikely to be detected in subsequent genotyping efforts. The allele-prevalence information that served as the basis of the original CWD catalogue derived from genotyping performed with sequence-specific oligonucleotide-probe (SSOP), sequence-specific primer (SSP), and DNA sequence-based typing (SBT) methods. At the time, these methods considered nucleotide polymorphisms located primarily in exon 2 of class II alleles and exons 2 and 3 of class I alleles. These exons encode the antigen-recognition domain (ARD) of the HLA protein, a domain that binds peptides, and interacts with T cell receptors and killer-cell immunoglobulin-like receptors. SSOP and SSP methods provide only partial sequence information for a given exon. While this approach was sufficient for developing a CWD catalogue specific for proficiency testing at the time, it was insufficient for developing a comprehensive understanding of allele prevalence, making the original CWD catalogue ill-suited to some of the applications for which it is currently being utilized.

The original CWD catalogue has proven an effective predictor of allele prevalence in many recent studies (e.g., 5–7). For example, Cano, Mack, and Fernández-Viña (8) determined the predictive value of the original CWD catalogue to range from 99.53–99.95 for the alleles proposed by He et al. (9) to be CWD in the Han Chinese population. However, the discrepancy between the intent with which the CWD catalogue was devised and the additional applications implemented by the histocompatibility and immunogenetics community suggests that an update to the catalogue is required. Several additional factors have also necessitated a close review of the original catalogue. Since the publication of the original CWD catalogue, the number of recognized alleles at the classical HLA loci has increased more than three-fold (10), and feedback received from the histocompatibility and immunogenetics community over the last five years has made it clear that some of these alleles may warrant inclusion in the catalogue. For example, the same studies in which the predictive power of the original CWD catalogue has been demonstrated (5–7,9) have also suggested that there remain some alleles (e.g., A*32:08 and C*07:13) that should be added to the catalogue. The extension of SBT methods to exons that do not encode the ARD, and

the application of these methods in populations that had not previously been extensively genotyped, has identified alleles that were unknown or could not be considered at the time that the original list was compiled (9,11). Finally, the original CWD catalogue is not available in a portable electronic form; it was published as a set of manuscript tables, and does not reflect the recent, and in some cases, non-obvious, changes that have been made to the nomenclature for HLA allele names (12).

A working group was convened in 2010 for the purpose of reviewing and updating the CWD catalogue; where the original catalogue was the product of an ASHI *ad-hoc* committee, this working group was expanded to include representatives from Asia, Europe, South America, and the Pacific. Rather than simply working to revise the original CWD catalogue, this working group set for itself the goals of developing new criteria for considering allele prevalence in light of technological and scientific innovations, and of identifying new ways to make the allele prevalence information compiled in the CWD catalogue available and useful to the research community. Here, we present a first update to the CWD catalogue.

Materials and Methods

Children's Hospital & Research Center Oakland's Institutional Review Board approved the collection and storage of allele and haplotype prevalence data that exclude human subjects identifiers for this research. The work described here involves coded private information, the data were not collected specifically for this research project, and investigators cannot determine the identity of individuals to whom these data pertain.

Allele Categorizations and Inclusion Criteria

The efforts of the working group began with the division of all 6632 alleles at the HLA-A, -B, -C, -DRB1, -DRB3/4/5, -DQA1, -DQB1, -DPA1 and –DPB1 loci in IMGT/HLA Database release 3.5.0 into three categories. Alleles were initially assigned to these categories on the basis of published studies (13–79), frequency data available in the Allele Frequencies Net Database (AFND) (80), allele prevalence data collected as part of the AFND rare alleles project (http://allelefrequencies.net/hla6001a.asp), version 3.1.0 of the National Marrow Donor Program's (NMDP) biannual rare alleles list (http://bioinformatics.nmdp.org/HLA/Rare_Allele_Lists/Biannual_Rare_Allele_Lists.aspx), and SBT results from the M.D. Anderson Cancer Center. Duplicate sources (e.g., published studies that are also in included in AFND) were considered only once.

The alleles in the first category have been observed in multiple populations, although not necessarily in every population or in every region of the world. We identify these alleles as being *common*, and call this the Common category. There is universal agreement about these alleles, their frequencies are known, and there is ample data supporting their presence and frequency. As described by Cano et al. (1), these alleles are observed at frequencies > 0.001 in reference populations of at least 1,500 individuals.

The alleles in the second category are not as widely distributed as the alleles in the Common category, but their presence has been documented in many studies. Their frequencies are less certain than those of alleles in the Common category. These alleles may be described as "rare" in some cases, but the term "rare" has been given a variety of conflicting definitions. For example, the AFND rare alleles project defines alleles that have been reported one to three times since they were initially identified as rare, and those alleles that have never been reported since their initial identification as very rare, whereas the NMDP biannual rare alleles list includes class I alleles observed at a frequency less than 1/50000 and DRB1 alleles observed at a frequency of less than 1/100000 in the NMDP registry. To avoid

confusion with these terms, we identify these alleles as being *well-documented*, and call this the Well-Documented category.

Alleles were included in the Well-Documented category if they had been observed five times in unrelated individuals through the use of a SBT method that assessed the pertinent exon(s), or if they had been detected three times via SBT and observed in a specific haplotype in unrelated individuals. For example, the predicted polypeptide sequence of A*23:17 differs from that of A*23:01:01 by an amino-acid H283P change encoded in exon 5. The A*23:17 allele has been identified in three unrelated individuals in the same ethnic group via exon 5 sequencing, and is associated with a B*45:01~DRB1*13:01 haplotype. Because this allele was identified in multiple individuals, persists in a population in a specific haplotype, but is not observed in numerous populations at high frequency, it was included in the Well-Documented category.

Much of the effort of the working group involved the consideration of the alleles that were not initially included in either the Common or Well-Documented categories. This work included the evaluation of alleles that were part of the original 2007 CWD catalogue, but for which prevalence data seem to be lacking, as well as alleles that were not included in the original 2007 CWD catalogue, but which may have merited inclusion in the Well-Documented category if sufficient support could be found for them. The working group was tasked with scrutinizing these alleles with the goal of providing support for their inclusion in the Well-Documented category.

Examples of these alleles include A*24:06, which was included as part of the original CWD catalogue, and A*11:53, which was not. The predicted polypeptide sequence of A*24:06 differs from A*24:02 by an amino-acid Q156W change encoded in exon 3. While this allele was reported 39 times in 10 studies deposited in the AFND, all of those studies used SSOP and SSP methods, and the complete exon 3 sequence of this allele appeared to have been identified in only one cell. Because the presence of this allele had been inferred from SSOP methods (and in at least 5 individuals in the population from which the original cell was derived), it was suggested for consideration by the working group.

The predicted polypeptide sequence of A*11:53 differed from that of A*11:02 by an amino-acid P276L change encoded in exon 5. This difference was particularly noteworthy in that the P276 of A*11:02 appeared to be an uncommon polymorphism that was not seen in other A*11 alleles, which display L276. We hypothesized that the relationship between A*11:02 and A*11:53 might have been comparable to that of DRB1*14:01:01 and *14:54:01; these alleles have experienced an inversion in perceived frequency in light of exon 3 polymorphism (81). A*11:53 may have warranted inclusion in the Common category, whereas, A*11:02:01 potentially warranted inclusion in the Well-Documented category, or possibly exclusion from the catalogue. It was subsequently discovered that the exon 5 sequence of A*11:02:01 contained an error, and that A*11:53 was identical to the corrected sequence of A*11:02:01 (11).

The working group was asked to identify any alleles excluded from the Common and Well-Documented categories that had been detected using a SBT method that assessed the appropriate unique sequence features. At the beginning of this effort, 5758 IMGT/HLA Database 3.5.0 alleles had not been included in the original CWD catalogue, and were not considered as candidates for inclusion in the Well-Documented category. For example, the nucleotide sequence of C*12:02:01 differs from that of C*12:02:02 by a nucleotide change (A873G) in exon 4. While C*12:02:01 had been reported 89 times in 16 studies deposited in the AFND, the genotyping performed in these studies assessed exon 2 and 3 data alone, and C*12:02:01 was reported because it is the lowest numbered allele in an ambiguity group that

also included C*12:02:02 (which was included in the Common category). Because of this, C*12:02:01 appeared to have only been identified in one cell.

SBT data for individual alleles and available haplotype association data were collected from the working group and used to assess the initial exclusion of alleles from the Well-Documented category. Alleles detected five times via SBT methods in unrelated individuals or that were detected three times via SBT in unrelated individuals sharing a haplotype, were assigned to the Well-Documented category. Alleles that did not meet these minimum threshold criteria were excluded from the catalogue. After these evaluations, the alleles in the Common and Well-Documented categories were compiled into the updated CWD catalogue presented here.

It is important to note that these criteria are more conservative than those described by Cano et al. (1), under which alleles were considered CWD if they were observed three times in unrelated individuals, regardless of the typing methodology employed. The aim in applying this more conservative approach was to exclude alleles from the CWD catalogue that may be generated and lost stochastically and that therefore do not persist in the human population. Klitz, Hedrick, and Louis (82) estimated that 3.5 million alleles exist at each HLA locus in the current human population and that 1.4 million of these are newly generated; many of these latter will likely not persist in the population, and should not be included in the CWD catalogue, but as SBT methods are more commonly used and as sequencing efforts are extended into additional sequence regions, the likelihood that they will be detected and included in the IMGT/HLA Database increases. The consistent appearance of an allele in a specific haplotype speaks to the presence of that allele in a population, suggesting that it is what Klitz et al. describe as “epidemiologically consequential.” Similarly, SBT methodology is crucial for allele detection with low levels of associated ambiguity, and as knowledge of allelic polymorphism is extended to new exons, introns and untranslated regions, SBT should be considered a standard method for estimating allele prevalence.

Finally, the common or well-documented categorizations and allele prevalence data collected for individual alleles were used to categorize G and P groups. A given G group represents all alleles that share a nucleotide sequence for ARD-encoding exons, and a given P group represents all alleles that share a polypeptide sequence for the ARD, excluding null alleles (12).

Results

The working group provided prevalence information on 1758 HLA-A, -B, -C, -DRB1, -DRB3/4/5, -DQA1, -DQB1, -DPA1 and -DPB1 alleles, representing 26.5% of the HLA alleles in IMGT/HLA Database release 3.5.0. Of these, 139,961 SBT observations were reported for 1572 alleles detected in Australia, Brazil, China, France, the Netherlands, and the United States of America. Details of these SBT observations are presented in Table 1. The updated CWD allele catalogue compiled from these data is presented in Supplementary Table S1; in addition to identifying each allele included in the updated catalogue and its common or well-documented status, this table identifies the IMGT/HLA Database accession number for each included allele, and identifies included alleles that were part of the original CWD catalogue, included alleles that were identified after IMGT/HLA Database release 2.15.0, and included alleles with names that were extended subsequent to IMGT/HLA Database release 3.5.0. The original CWD catalogue published by Cano et al. (2007) is hereafter referred to as the CWD 1.0.0 catalogue, and the update to the catalogue described here as the CWD 2.0.0 catalogue. Details of this version identification system are provided below. Although these allele prevalence evaluations were performed on IMGT/HLA

Database 3.5.0 alleles, the allele-names have been updated to those in IMGT/HLA Database release 3.9.0. The names of 20 alleles were extended through the addition of an extra polymorphic field between the release of IMGT/HLA Database 3.5.0 and 3.9.0; in these cases, the sequence of the allele included in the CWD 2.0.0 catalogue is consistent with the SBT data provided by the working group.

A comparison of the allele content of the CWD 1.0.0 and 2.0.0 catalogues is presented in Table 2. The CWD 2.0.0 catalogue includes 1122 alleles whereas the CWD 1.0.0 catalogue included 721; however 33 alleles in the CWD 1.0.0 catalogue are absent from the CWD 2.0.0 catalogue, so that 434 alleles have been added to the CWD catalogue. Of these, 82 alleles were identified subsequent to IMGT/HLA Database release 2.15.0 and could not have been included in the CWD 1.0.0 catalogue. The 33 alleles that have been removed from the CWD catalogue are presented in Table 3. The remaining 6712 alleles at the HLA-A, -B, -C, -DRB1, -DRB3/4/5, -DQA1, -DQB1, -DPA1 and –DPB1 loci in IMGT/HLA Database release 3.9.0 have been excluded from the CWD catalogue.

The CWD 2.0.0 catalogue for G groups is presented in Supplementary Table S2, and the CWD 2.0.0 catalogue for P groups is presented in Supplementary Table S3. Of the 151 G groups that can be derived from IMGT/HLA Database 3.9.0 alleles, only 4 (A*02:81:01G, B*15:123:01G, B*35:137:01G and C*07:01:20G) are excluded from the CWD 2.0.0 catalogue. Of the 147 G groups included in the CWD 2.0.0 catalogue, 142 include at least one common allele, while only five included no common alleles.

Of the 415 P groups that can be derived from IMGT/HLA Database 3.9.0 alleles, 290 were included in the CWD 2.0.0 catalogue; of these, 241 include at least one common allele, while 48 included no common alleles. Only one P group (C*04:15P) in the CWD 2.0.0 catalogue included only alleles that had individually been excluded from the catalogue; this P Group comprises three such alleles (C*04:15:01, *04:15:02 and*04:15:03), but is included in the CWD 2.0.0 catalogue because C*04:15:01 and *04:15:02 were identified six times in total via SBT methods; where these alleles individually did not meet the threshold for inclusion of five SBT observations, the exon 2 and 3 sequence represented by this P group did. This is the only P group in the CWD catalogue for which this is the case.

Discussion

We have updated the CWD catalogue using SBT observations of alleles in Australia, East Asia, Europe, and the Americas. This CWD 2.0.0 catalogue includes 14.3% of the HLA-A, -B, -C, -DRB1, -DRB3/4/5, -DQA1, -DQB1, -DPA1 and -DPB1 alleles in IMGT/HLA Database release 3.9.0. More than 95% of the alleles in the CWD 1.0.0 catalogue were included in the CWD 2.0.0 catalogue, and, though a more conservative set of inclusion criteria were applied for well-documented alleles than previously, the overall size of the catalogue has increased by 56%. Of the 6712 alleles excluded from the CWD 2.0.0 catalogue, 337 were observed two, three or four times (data not shown), suggesting that the number of alleles in the catalogue may increase in the future. We have also categorized G and P groups, in terms of the aggregate prevalence of their constituent alleles, for the first time. While 97% of G groups are CWD, only 70% of P groups are. However, these CWD P groups represent 88% of the alleles in the CWD 2.0.0 catalogue.

Applications of the CWD 2.0.0 Catalogue

The CWD 1.0.0 catalogue was created for use with proficiency testing. Given that the CWD 2.0.0 catalogue distinguishes common alleles from well-documented alleles, and extends these categories to G and P groups, we envision that the histocompatibility and

immunogenetics community will extend the CWD 2.0.0 catalogue to a variety of distinct research and clinical applications.

In updating this catalogue, we have endeavored to provide a more comprehensive snapshot of allele prevalence based primarily on SBT methodology, but the catalogue remains a snapshot, and we assume that future advances in genotyping methods and our understanding of functionally important HLA polymorphisms will inform the composition of future catalogues. This CWD 2.0.0 catalogue is likely more useful than the CWD 1.0.0 catalogue for applications that depend on allele prevalence information – the reduction and resolution of ambiguity for research and clinical practice, the identification of potential matches for transplantation, and the general management of allele-data in the face of an ever growing list of recognized allele sequences.

For example, HLA typing results for a given individual may be consistent with multiple alternative genotypes for a given HLA locus. In the evaluation of the typing results for a heterozygous individual, a genotype that includes one CWD allele and one non-CWD allele should signify the need to review potentially spurious nucleotide base calls, or probe or primer reactivities.

In research studies of disease association with HLA polymorphism, the CWD 2.0.0 catalogue may be useful for identifying the genotype that is most likely to be present in a given subject; the identification of such ‘CWD-resolution genotypes’ may allow for more straight-forward gene frequency calculations in patient and control groups.

When histocompatibility testing for allogeneic hematopoietic stem-cell transplantation (HSCT) between unrelated individuals, it is essential to define the level of resolution of the HLA typing performed. The Harmonization of Histocompatibility Typing Terms Working Group recently defined a high-resolution typing result ‘as a set of alleles that encode the same protein sequence for the region of the HLA molecule called the antigen binding site and that exclude alleles that are not expressed as cell-surface proteins’ (83). This definition coincides with the definition of the P groups of alleles defined by The WHO Nomenclature Committee for Factors of the HLA System in 2010 (12). P groups encode identical antigen recognition domains with the aim of fully assessing the match grade between the patient and the unrelated donor while avoiding any ambiguity at a functional level. Supplementary Table S3 identifies the P groups that include at least one CWD allele; this catalogue of CWD P groups should prove particularly useful, as the vast majority of patients seeking an unrelated donor will present either unambiguous HLA typing results or ambiguous results in which one allele belongs to a P group.

The CWD 2.0.0 catalogue may be applied by transplant programs, registries of volunteers HSCT donors and cord blood banks to determine the minimal resolution requirements for HLA typing tests in the same manner that Cano et al. (1) originally recommended the use of the CWD 1.0.0 catalogue for evaluating proficiency tests. This original recommendation was that an acceptable proficiency testing result includes either a single unambiguously assigned possible genotype, or multiple ambiguous genotypes in which only one genotype includes two alleles in the CWD 1.0.0 catalogue, whereas the other alternative genotypes do not include any CWD alleles.

Apropos of this original recommendation, we propose that accreditation organizations such as ASHI and the European Federation for Immunogenetics collaborate to identify a catalogue of alleles that are appropriate for use in clinical practice. This can be the CWD 2.0.0 catalogue, or another catalogue developed by these societies for this purpose. Rather than requiring that a typing result includes all possible ambiguous genotypes associated with a given pair of ARD-encoding exon sequences, accreditation organizations could restrict

reports to alleles in the catalogue. For example, the ambiguous genotype combinations that correspond to the four ARD-encoding exon sequences represented by the A*02:01:01G and A*03:01:01G G groups includes 555 genotypes when these G groups are expanded to their constituent alleles. The number of genotype combinations in this case can be considerably higher when an SSOP or SSP method is employed rather than an SBT method. However, of these 555 genotypes, only 11 involve both an A*02 and A*03 allele in the CWD 2.0.0 catalogue.

Since the publication of the CWD 1.0.0 catalogue, the clinical HLA typing community has observed patients and donors with ambiguous HLA types that include one or two CWD alleles in more than one of the possible genotypes. In some cases, there may not be simple or feasible methods available to resolve some ambiguous genotypes, and in these cases the expert evaluation of haplotypic associations may help to determine which genotype is the most likely. We envision that future versions of the CWD catalogue will include multi-locus haplotypes that include CWD alleles along with their distribution in the human population.

CWD Catalogue Update Schedule

The CWD catalogue will be updated on a regular basis, with successive updates identified via a three-field version number (e.g., CWD 1.0.0 catalogue and CWD 2.0.0 catalogue). Major updates, consisting of changes to the category status of alleles and the addition and removal of alleles to and from the catalogue based on input from the histocompatibility and immunogenetics community, will occur in conjunction with the International HLA and Immunogenetics Workshops (IHIW); these updates will be reflected in the first field of the version number, and the next such update will take place in 2016, as part of the 17th IHIW.

Minor updates, consisting of changes made to allele names as recorded in the IMGT/HLA Database, will be made annually; these updates will be reflected in the second field of the version number, and the next such update will take place at the end of 2013. Because major category changes will not be made on an annual basis, we anticipate that these minor updates will pertain to allele names that have been deleted, renamed, or extended to reflect new polymorphisms (e.g., the extension of an allele name through the addition of an additional field or an expression variant character), as well as the addition or modification of accessory information for specific alleles (e.g., identifying alleles specific to particular populations or regions of the world, or observed in particular haplotypes).

Any errors in the catalogue will be updated as necessary; error-correction updates will be reflected in the third field of the version number.

Electronic Access and Community Input

The CWD 2.0.0 catalogue is available online at cwd.immunogenomics.org; future updates will be made available on this site as well. In addition, the CWD catalogue will be integrated into the AFND (www.allelefrequencies.net), and the IMGT/HLA Database (www.ebi.ac.uk/ipd/imgt/hla/). The NMDP will replace the biannual rare alleles list with a list of alleles that have been excluded from the CWD catalogue; this list will be updated on a quarterly basis. Input from the histocompatibility and immunogenetics community regarding the composition of the catalogue and suggestions for future updates is welcomed, and can be submitted via email to cwd@immunogenomics.org.

Looking forward to future updates of the CWD catalogue, it is clear that SBT efforts will extend into new sequence regions that have not previously been characterized, and that many new polymorphisms will be detected. This will result in a further acceleration of new allele discovery, with corresponding increases in ambiguity. As Klitz et al. (82) have noted, many of these new alleles will be unique, and of little consequence epidemiologically. In

order to appropriately assess the prevalence of these new variants, certain knowledge of the number of times that a sequence has been observed will be required. Toward this end, it will be crucial that SBT confirmations of alleles that have not been included in the CWD catalogue be transmitted to the IMGT/HLA Database and reported to the community. Multi-locus haplotypes (e.g., as inferred from family-studies) can provide a chromosomal context for understanding allele prevalence, and should also be reported in a standard and routine fashion. There persists within the histocompatibility and immunogenetics community a certain excitement surrounding the identification and publication of a novel allele sequence, but in many ways the confirmation of known sequences is more important.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by National Institutes of Health (NIH) grant U01AI067068 (JAH and SJM) awarded by the National Institute of Allergy and Infectious Diseases (NIAID). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Allergy and Infectious Diseases or the NIH. Australian governments fully fund the Australian Red Cross Blood Service for the provision of blood products and services to the Australian community. We thank Dawn R. Wagenknecht for her participation in the CWD working group, Marilyn S. Pollack for sharing her experiences regarding allele prevalence, and Henry A. Erlich for his thoughtful discussions and careful proofreading of this manuscript.

Abbreviations

AFND	Allele Frequencies Net Database
ARD	Antigen-Recognition Domain
ASHI	American Society for Histocompatibility and Immunogenetics
CWD	Common and Well-Documented
HLA	Human Leucocyte Antigen
HSCT	Hematopoietic Stem Cell Transplantation
IHIW	International Histocompatibility Workshops
IMGT	IMmunoGeneTics
NMDP	National Marrow Donor Program
SBT	Sequence Based Typing
SSOP	Sequence-Specific Oligonucleotide Probe
SSP	Sequence-Specific Primer

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Table 1

Sequence-Based Typing Observations Provided by the Working Group

Source Nation	Number of Reported Alleles	Number of SBT Observations	Number of Unique SBT Observations	Number of Alleles in the Updated CWD Catalogue
Australia	116	179	75	63
Brazil	14	41	0	13
China	238	21444	69	210
France	15	26	13	10
Netherlands	78	226	47	33
United States[a]	1431	118045	449[b]	893

[a] Data from the United States of America were provided by five laboratories.

[b] Each of these alleles was observed in only one of the five participating laboratories from the United States of America.

Table 2

Comparison of the CWD 1.0.0 and 2.0.0 Catalogues

Locus	Number of CWD 1.0.0 Alleles	Number of CWD 2.0.0 Alleles	Number of CWD 2.0.0 Common Alleles	Number of CWD 2.0.0 Well-Documented Alleles	Number of Alleles Shared Between CWD 1.0.0 & 2.0.0
A	130	246	68	178	123
B	245	367	125	242	235
C	81	146	44	102	77
DRB1	142	226	79	147	139
DRB3	14	12	5	7	9
DRB4	7	8	6	2	7
DRB5	8	8	5	3	8
DQA1	16	19	15	4	16
DQB1	27	30	22	8	25
DPA1	0	6	6	0	0
DPB1	51	54	40	14	48
Total	721	1122	415	707	687

Table 3

HLA Alleles Removed From the CWD Catalogue

Locus	IMGT/HLA Accession Number	IMGT/HLA 3.9.0 Allele Name
A	HLA01038	A*23:02
	HLA00969	A*24:21:01
	HLA01268	A*24:28
	HLA00077	A*26:05
	HLA00087	A*29:03
	HLA00120	A*68:04
	HLA00128	A*74:02:01:01
B	HLA01763	B*07:02:04
	HLA01725	B*07:32
	HLA01230	B*08:12:01
	HLA01486	B*13:09
	HLA01912	B*15:86
	HLA00291	B*40:01:01
	HLA01452	B*41:06
	HLA02098	B*44:41:01
	HLA01953	B*47:05
	HLA02201	B*58:11
C[a]	HLA00408	C*02:03
	HLA01472	C*02:05
	HLA01831	C*04:04:02
DRB1	HLA00703	DRB1*04:17:01
	HLA00753	DRB1*11:01:03
	HLA00781	DRB1*11:27:01
DRB3	HLA01191	DRB3*01:01:02:02
	HLA00900	DRB3*02:07
	HLA01095	DRB3*02:09
	HLA01560	DRB3*02:16
	HLA00904	DRB3*03:03
DQB1	HLA00657	DQB1*06:11:02
	HLA01460	DQB1*06:19
DPB1	HLA00544	DPB1*26:01:01
	HLA00569	DPB1*50:01
	HLA01947	DPB1*102:01

A: The Cw*0502 allele was included in the CWD 1.0.0 catalogue, but was determined to be identical to the Cw*0509 allele (now C*05:09) as part of IMGT/HLA Database release 2.19.0.