# WMDA

## Search Tools Guide

Educational. Expert Led. E-Learning.

education.wmda.info

# Table of Contents

## Introduction

Search and selection of donors and cord blood units (CBU) for your patient is a conscientious job. You often start with analysing the patient's HLA results and searching in the global WMDA Search & Match Service or in your own registry database. If many donors or CBUs have been genotyped at high resolution, the selection might not so difficult, although you still can consider many secondary selection criteria like, blood group, CMV and gender.

However, when you can only find potential matched donors or CBUs genotyped at low or intermediate resolution and /or genotyped for just a few loci, a more extended analysis is required to be able to predict and select the best donors or CBUs and give deliberate advise to the physician of the patient.

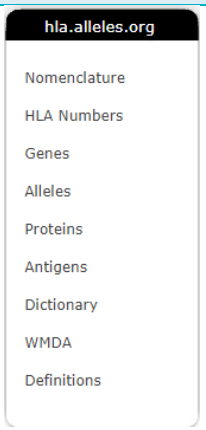
Although the Search & Match Service gives you probabilities of matching for loci that have not been genotyped or at lower resolution, you have to keep in mind that these probabilities are mainly based on geographical location of the donor/CBU because ethnicity data is often unknown. The probabilities might therefore deviate depending on the actual ethnicity of the donor/CBU.

For extended analysis of your patient's HLA and the HLA of potentially matched donors/CBUs, you can use multiple tools to investigate for example allele frequencies, haplotypes, haplotype associations, and global distribution of alleles.

Within this search tools guide, we explain different search tools and websites that can be useful during your search and selection process. At the end of the guide, we added two summary tables for quick selection of the search tool or website you need. One table is based on the order of the search tools in this guide and the second table is a kind of decision tree and is subdivided in different topics with their corresponding websites.

We hope this search tools guide might assist you during future donor/CBU search and selection procedures and helps you to generate well considered advise reports with the best potentially matched donors/CBUs for your patients.

## HLA Nomenclature

| Website address | http://hla.alleles.org/nomenclature/index.html | |
|---|---|---|
| **What can I find here?** | This website contains information on HLA nomenclature and all valid/invalid alleles and groups of alleles. It is mainly a source of information rather than a real search tool. | |
| **Navigation on website** | On the left side, you can find the main menu/navigation bar with the specific areas the website comprises.<br>For every area in this menu, submenus show up on the top of the page, just below the nomenclature banner (shown in figure 1) |  |

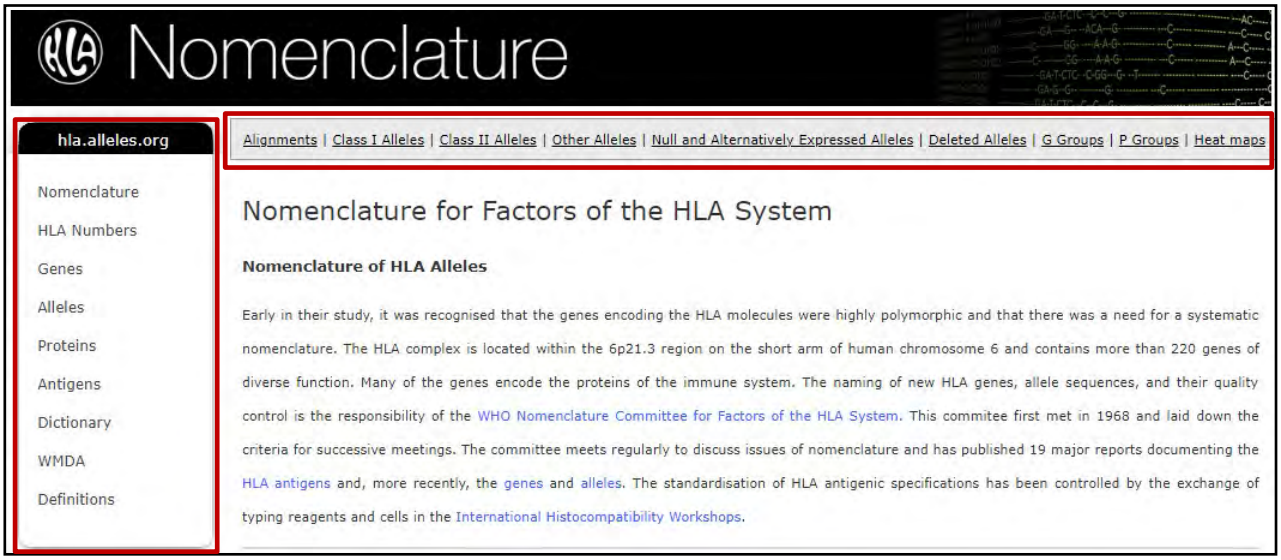


Figure 1: Submenu structure on the Nomenclature page. Navigation shown in red boxes at the left and on top of the page.

This website includes a lot of useful information on HLA nomenclature and also the current valid and invalid HLA alleles. The following list includes the information you can find on this website based on the main menu on the left side on the website.

**Nomenclature**, including:

- Full lists of HLA Class I and Class II valid alleles
- Null alleles and alternatively expressed alleles
- Deleted alleles (no longer valid)
- G groups: List of G codes with the alleles (same nucleotide sequence in exons encoding for the peptide binding domains) within that group
- P groups: List of P codes with the alleles (same antigen binding domains) within that group

**HLA Numbers**, including:

- How many different HLA alleles are known
- Explanation on how an allele is named
- Nomenclature publications, nomenclature update files, information on the nomenclature committee

**Genes**: Table with all HLA genes
**Alleles**, including:

- HLA alleles sequence information
- Same submenu as nomenclature

**Proteins**, including:

- Full lists of Class I and Class II HLA proteins
- P groups

**Antigens**, including:

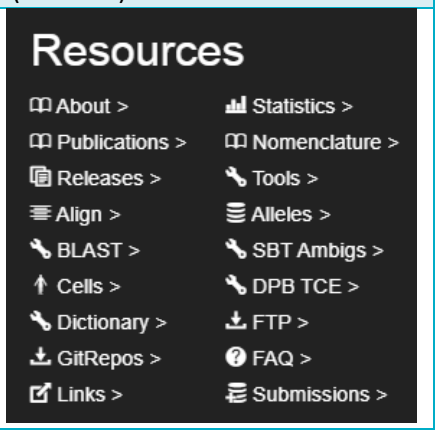
- Nomenclature of serologically defined HLA antigens
- List of all officially recognised HLA antigens
- List of broad, split and associated antigens
- Specific information on Bw4 and Bw6
- Previous names of WHO HLA antigen assignments

**Dictionary**: links to publication of the HLA dictionary 2008
**WMDA**: 5 files including information on the official WHO nomenclature, relationship between defined antigens, relationship between allele sequence and serologically defined antigens.
**Definitions**: publications on definitions and standards

On the top menu, you can find quick access to the following topics, which might be also covered in menus described above:

- **Alignments:** Sequence alignments (nucleotide/genomic/peptide) of all alleles per locus.
- **Class I Alleles:** Full list of HLA Class I alleles.
- **Class II Alleles:** Full list of HLA Class II alleles.
- **Other Alleles:** Other than Class I and Class II alleles.
- **Null and Alternatively Expressed Alleles:** HLA alleles that have been shown to be either not expressed (Null alleles that have the suffix 'N'), or the alleles that have been shown to be alternatively expressed have the suffix 'L', 'S', 'C', 'A' or 'Q'.
- **Deleted Alleles:** Allele names that have been deleted from the official WHO HLA Nomenclature
- **G Groups:** HLA alleles that have identical nucleotide sequences across the exons encoding the peptide binding domains
- **P Groups:** P Codes For HLA alleles having the same antigen binding domains
- **Heat maps:** These heat maps look at the amino acids seen at each position for some of the main HLA genes and graphically display the levels of polymorphisms seen.

## IPD-IMGT/HLA database

| Website address | https://www.ebi.ac.uk/ipd/imgt/hla/ | |
|---|---|---|
| **What can I find here?** | This website from the European Bioinformatics Institute includes the IPD-IMGT/HLA database with sequences of the major histocompatibility complex (MHC) and several related tools, like<br>• Sequence Alignment Tool (Align)<br>• Basic Local Alignment Search Tool for protein or nucleotide sequences (BLAST)<br>• HLA Dictionary (Dictionary)<br>• Query tools (Tools)<br>• Ambiguous allele combinations (SBT Ambigs)<br>• DPB1 T-cell epitope algorithms (DPB TCE) | |
| **Navigation on website** | On the right side, you can find the main menu/navigation bar with the specific areas the website comprise.<br>For every area in this menu, submenu's sometimes show up on the page itself. |  |

### Alignment tools: Align and BLAST

**Align:** https://www.ebi.ac.uk/ipd/imgt/hla/align.html

With this tool you can align a specific sequence to a reference HLA allele sequence.

**STEP 1**

- In the first box, specify the locus of your reference HLA gene.
- At the box 'features' choose the type of sequence; so DNA nucleotides, protein regions, a certain specific exon or intron.

**STEP 2**

- Specify in the third box the reference sequence/allele.
- In the box 'specific sequences required' you can add a specific allele or alleles, but you can also leave it empty resulting in alignment of all known alleles on this locus to your reference allele.

**STEP 3**: Select alignment display options:

- Mismatches: only nucleotides (bases) of mismatches are shown or all nucleotides (bases) are shown-> 2nd option is more difficult to identify differences.
- Numbering: in codons (triplet of nucleotides coding for an amino acid) or in blocks of 10 nucleotides.

- Alleles unsequenced in selected region: you can omit the alleles that are not sequenced over the region of interest from their alignment. This will reduce the time taken to perform the alignment. For some loci, genomic alignments can contain over 1.5 million bases if all sequences are selected. When non-coding regions are selected, all alleles which contain unsequenced regions are removed from the alignment by default. Where possible, select only the sequences needed as this will reduce the loading time and make the alignments easier to view.
- Output: choose the output format of your results; either text or with hyperlinks.

**STEP 4**: Click on the 'Align Sequences Now' button.

More information can be found in the help document:
https://www.ebi.ac.uk/ipd/imgt/hla/help/align_help.html

**BLAST: https://www.ebi.ac.uk/Tools/sss/ncbiblast/**

With this tool you can align a nucleotide sequence or a protein sequence to a database of known sequences.

- Depending on the type of sequence you would like to align, click on the link of the corresponding Blast Search tool: Protein or Nucleotide Blast Search

Within the Blast tool:

**STEP 1**: Select the database in which you would like to search.
**STEP 2**: Paste or upload your sequence.
**STEP 3**: Set parameters; default is often OK for most users.
**STEP 4**: Submit your search by clicking on the 'submit' button. You can also choose to be informed by email when the results are available.

## HLA Dictionary

**HLA Dictionary: https://www.ebi.ac.uk/ipd/imgt/hla/alleles/dictionary/**

With this tool you can retrieve information on HLA alleles. The tables list the alleles with remarks on the serologic patterns and the equivalents. The serological equivalents are listed as expert assigned types, and the data are useful for identifying potential stem cell donors who were typed by either serology or DNA-based methods.

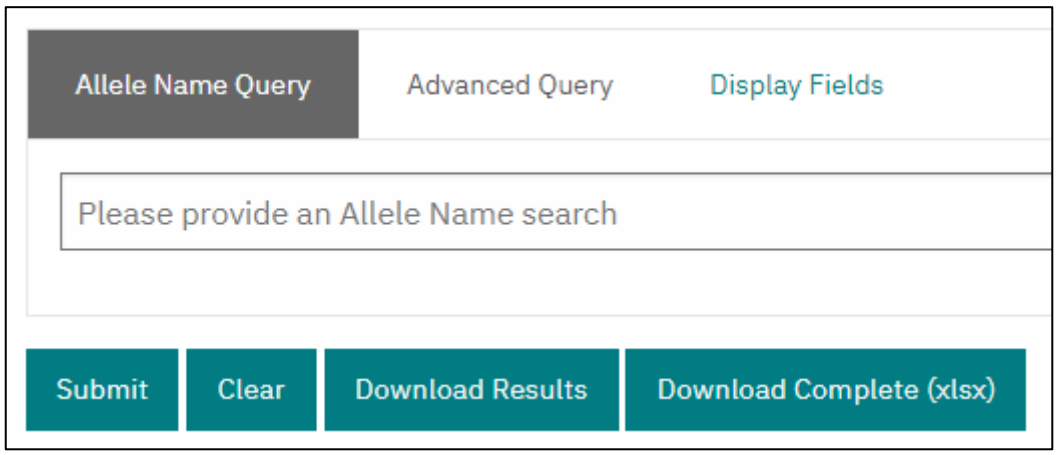



Figure 2: Search box for the HLA Dictionary.

**STEP 1**: Select your type of search: HLA Allele, Expert Assigned type or WHO Assigned Type. Use either the option 'Expert Assigned Type' or 'WHO Assigned Type' for searching to a serological value and 'HLA Allele' for searching to allelic values.

**STEP 2**: Specify your search determinant in the second field; an HLA gene, like A, an allelic value, like A*01, A*01:01 or serological value like B60.

**STEP 3**: Click on the 'Search the HLA Dictionary' button to start the search.
The results include information from different sources. Example from search for A*02:01 is shown in figure 3.

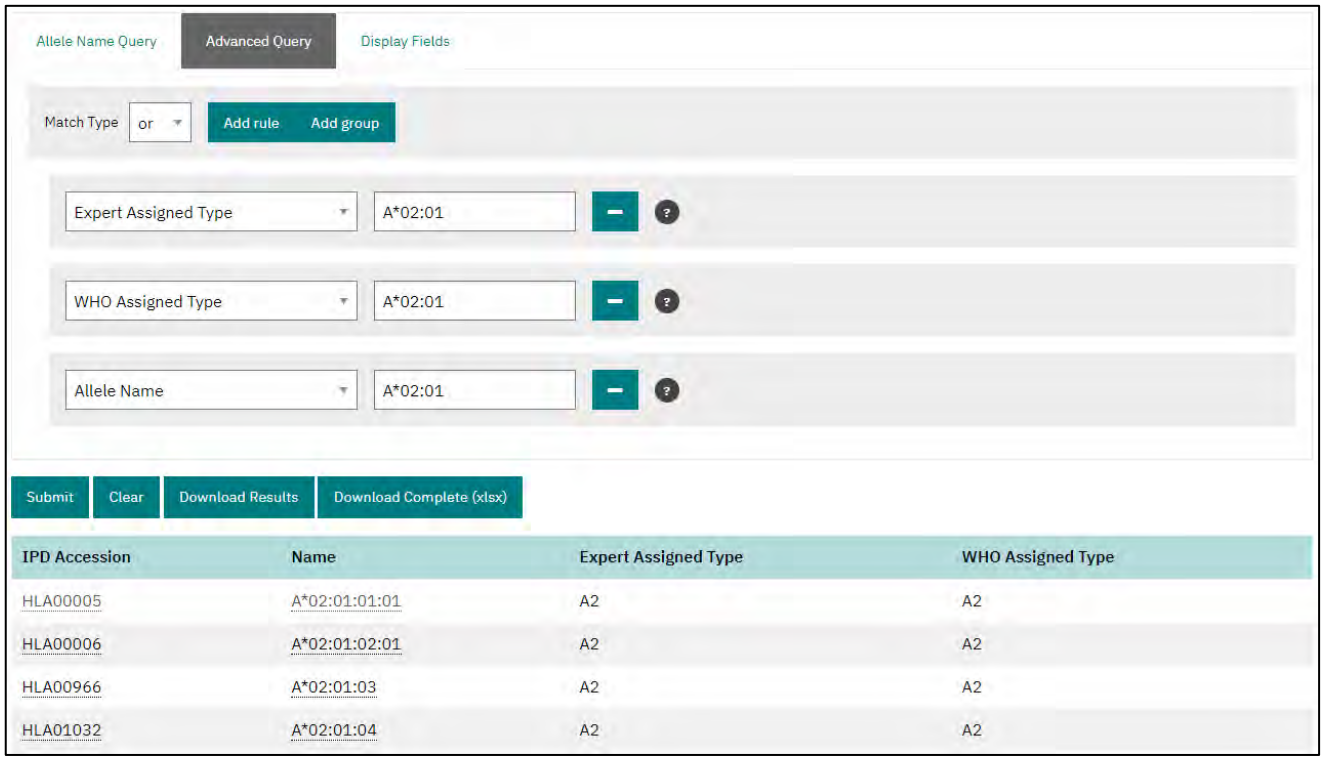
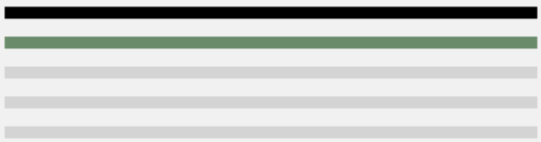



Figure 3: Results of a search in the HLA dictionary for HLA-A*02:01.

When you click on the link of the HLA allele, you can also retrieve an allele report. The first part of such a report is shown on the next page in figure 4. The nucleotide and genomic sequences are included in this report as well.

# Allele Report for A*02:01:01:02L

| A*02:01:01:02L | | | View HGVS Report |
|---|---|---|---|
| Pre-2010 Nomenclature: | A*02010102L | Local Names: | HLA*A2 expression variant |
| IMGT/HLA Acc No: | HLA01785 | OMIM Entry: | *142800 |
| Assigned: | 2003-07-31 | Sequence Last Modified: | 2003-10-15 |
| Source Entries: | AJ575565 , AM286552 , U02935 | | |
| Alignment of CDS Source Entries | A*01:01:01:01<br>A*02:01:01:02L<br>Submission 1<br>Submission 2<br>Submission 3<br>  <br>Locus Reference Virtual entry for A*02:01:01:02L Individual submission(s) | | |
| Cells Sequence Derived From: | CTM-77 , Gaff , PER(II.2) | | |
| Known Ethnic Origin Of Source: | Caucasoid | | |
| CWD v2.0 Status: | Not defined | | |
| ISO OID: | 2.16.840.1.113883.13.252 (HL7 Registered Organisational OID)<br>2.16.840.1.113883.13.252.1.1.1785 (Allele OID) | | |

**Publications**

Perrier P *et al. Tissue Antigens 68:442-5 2006.* (View abstract)
Balas A *et al. Hum Immunol 41:69-73 1994.* (View abstract)

**Confirmatory Data**

| Sequence Status: | Complete CDS | Confirmed: | Confirmed |
|---|---|---|---|
| Cells: | 3 | Laboratories: | 3 |

**HLA Dictionary Data**

| Expert Assigned Type: | Low A2 | WHO Assigned Type: | Low A2 |
|---|---|---|---|
| Tested by: | | No. Cells Tested: | Assigned Type: |
| International Cell Exchange UCLA (2008) | | - | - |
| NMDP (2008) | | - | - |
| 13 IHWC (2002) | | - | - |
| Neural Network Assigned Type: | | Identical to A*0201 | |
| Comments: | significantly reduced or low cell surface expression | | |

**Protein Sequence (365 aa)**

MAVMAPRTLVLLLSGALALTQTWAGSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEG
PEYWDGETRKVKAHSQTHRVDLGTLRGYYNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIALKEDLRSWTAA

Figure 4: First part of an allele report for HLA-A*02:01:01:02L.

More information about the results can be found on the following page:
**https://www.ebi.ac.uk/ipd/imgt/hla/alleles/dictionary/help/**

## Ambiguous Allele Combinations

**Ambiguous Allele Combinations: https://www.ebi.ac.uk/ipd/imgt/hla/ambiguity/help/**

The documents here include a list of all alleles that are identical over exons 2+3 for HLA class I and all alleles that are identical over only exon 2 for HLA class II. This page includes a search tool to search for a specific allele and files for download including all ambiguous alleles.
Why is such a list created? Due to the heterozygous nature of HLA sequencing analysis, the combinations of many pairs of alleles may give an ambiguous typing result.

## DPB1 T-Cell Epitope Algorithms

**DPB1 T-Cell Epitope Algorithms: https://www.ebi.ac.uk/ipd/imgt/hla/matching/**

Classification of HLA-DPB1 mismatches based on T-cell-epitope Groups (TCE-Groups) has been shown to identify mismatches that might be tolerated (permissive) and those that would increase risks (non-permissive) after unrelated donor haematopoietic stem cell transplantation (HSCT). These calculators allows you to enter the HLA-DPB1 typing of a patient and donor and view the predicted T-Cell epitopes and resulting prediction of the effect of mismatching when selecting specific donors for an HSCT recipient.

On this website, there are two versions of the prediction model, based on studies and publications. Some predicted TCE groups might differ between these two version.

The TCE prediction shown in the search results of WMDA Search & Match Service is based on a different prediction model and might differ from the model presented here by the IPD-IMGT website.

## Tools

**Tool: https://www.ebi.ac.uk/ipd/imgt/hla/about/tools/**

This page shows you multiple tools that you might consider to use during your donor/CBU search and selection. It includes query tools, submission tools, other EBI search tools, and phylogenetic analysis. The query tools might be most useful in the search and selection of a matched donor/CBU.

**Query Tools:**

- Allele Query form: Search tool for retrieving information on any allele in the IPD-IMGT/HLA Database. You receive an allele report as shown in figure 4 on page 9.
- Allele Status Checker: Allows users to determine which alleles contain only partial sequences and which alleles have not been independently confirmed.
- Conversion Tools: Tool for converting allele names to the new nomenclature. (e.g. A*01:01:02 vs A*010102)
- Deleted Alleles: List of deleted allele names, with reason for deletion.
- Ethnic Origins/ HLA Allele Ethnicity Tool: with this tool you can look up the ethnicity of individuals in which an allele was identified.
- KIR Ligand Calculator: Defines HLA-B and HLA-C ligand motifs associated with NK cell alloreactivity.
- Polymorphism Search Tool: Search tool to identify polymorphic positions in HLA sequences.

## Releases

**Releases: https://www.ebi.ac.uk/ipd/imgt/hla/release/**

This page contains quarterly reports of new, modified, and deleted sequences.
In the report, you can find the following sub-groups of sequences:

- New Sequences
- Sequences Pending
- Modified and Extended Sequences
- Corrected Sequences
- Deleted Sequences

## Common and Well-Documented Alleles

| Website address | https://www.ihiw18.org/component-immunogenetics/download-common-and-well-documented-alleles-3-0/ |
|---|---|
| **What can I find here?** | Common and Well-Documented (CWD) Alleles catalogue<br>This catalogue shows if an allele is common and well-documented or rare. |
| **Navigation on website** | The catalogue can be downloaded and is available in excel file format. |

NOTE: The following explanation is based on the catalogue when downloaded in excel file format.

**STEP 1**: Download the catalogue of interest in excel file format by clicking the link at the bottom of the page.

Version 3.0.0 catalog of common, intermediate and well-documented (CIWD) HLA-A, -B,-C, -DRB1, -DRB3, -DRB4, -DRB5, -DQB1 and -DPB1 alleles has been compiled from over 8 million individuals using data from 20 unrelated hematopoietic stem cell volunteer donor registries.

Version 1.0.0 of the CWD catalogue was published by Cano et al. (2007). Version 2.0.0 of the CWD catalogue was published by Mack et al. (2013) and pertains to the HLA-A, HLA-B, HLA-C, DRB1, DRB3, DRB4, DRB5, DQA1, DQB1, DPA1, and DPB1 alleles, as well as to the G and P groups at these loci. Other catalogues of CWD include that published by Sanchez-Mazas et al. (2017) focused on European populations and He et al. (2018) focused on the Chinese unrelated hematopoietic stem cell registry.

Differences of CIWD version 3.0.0 from earlier versions include:

- Based on IMGT/HLA version 3.31.0 database (January 2018)
- More global in scope
- Based on 14-15 million alleles at each locus, identified by DNA sequencing
- Because consecutive individuals, provides denominator allowing frequency to be calculated
- Common category is broader, captures more alleles; additional category added (intermediate) (C>I>WD)
- Primary data are available for further analysis

| Supplemental Table 5a (revised): HLA-A G and G Equivalent CIWD Frequencies [a] | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 3.0.0 CIWD Category by Population Group [b,c] | | | | | | | | |
| HLA-A IPD-HLA/IMGT 3.31. | Nomenclature Designation | AlleleID | Highest Frequency | Total | AFA | API | EURC | MENA | HIS | NAM | UNK |
| A*01:01:01G [d] | G | | C | C | C | C | C | C | C | C | C |
| A*01:01:02 | G | HLA01244 | WD | WD | | | WD | | | | |
| A*01:01:03 | G | HLA01971 | I | WD | | WD | I | | | | |
| A*01:01:05 | G | HLA03131 | WD | WD | | | WD | | | | |
| A*01:01:10 | G | HLA04427 | WD | WD | | | WD | | | | |
| A*01:01:11 | G | HLA04470 | WD | WD | | | WD | | | | WD |
| A*01:01:13 | G | HLA04558 | WD | WD | | | WD | | | | |
| A*01:01:16 | G | HLA05319 | WD | WD | | | WD | | | | |
| A*01:01:18 | G | HLA05332 | WD | WD | | | WD | | | | |
| A*01:01:21 | G | HLA05662 | WD | WD | | | | | | | |
| A*01:01:22 | G | HLA05684 | WD | WD | | | WD | | | | |
| A*01:01:29 | G | HLA05968 | WD | WD | | | WD | | | | |
| A*01:01:33 | G | HLA06097 | WD | WD | | | WD | | | | |
| A*01:01:34 | G | HLA06103 | WD | WD | | | | | | | |
| A*01:01:47 | G | HLA07994 | WD | WD | | | WD | | | | |
| A*01:02 | G | HLA00002 | C | C | C | I | C | C | C | C | C |
| A*01:03:01G | G | | C | C | C | C | C | C | C | WD | C |
| A*01:06 | G | HLA01031 | C | I | | | I | C | I | | I |

Figure 5: Overview of the columns in HLA G group catalogue.

## Be the Match /NMDP

| Website address | https://bioinformatics.bethematchclinical.org/ |
|---|---|
| **What can I find here?** | This website from the NMDP/Be the Match contains information on the following topics:<br>• Allele/haplotype frequencies in USA population<br>• Haplotype tool: HaploStats<br>• Allele code lists (incl. multiple-allele codes and CWD allele lists)<br>• CT policies<br>• MAC Service UI (previously known as DNA Type Lookup Tool) |
| **Navigation on website** | Navigation is on the top of the page; most useful information for you is within the HLA resources menu. (Figure 6) |

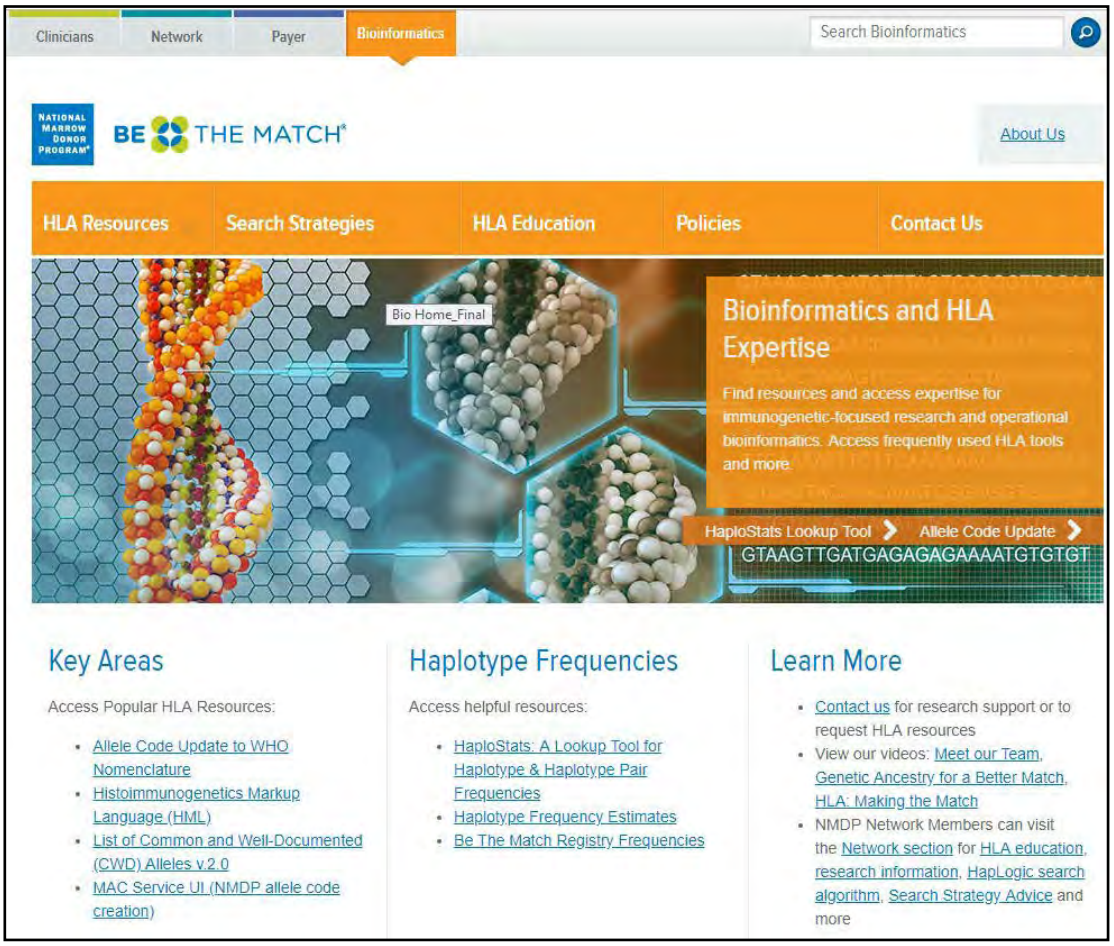


Figure 6: Be the Match website and menu structure.

### Haplotype Frequencies

**Haplotype Frequencies: https://bioinformatics.bethematchclinical.org/hla-resources/haplotype-frequencies/**

This page includes haplotype associations and allele frequency data for various race and ethnic populations determined within the US donor population. You can also find a link to haplotype frequency

information on the Jewish population from the Hadassah registry (Israel).

For every set of haplotype frequencies, you can download files (pdf or excel) with allele frequencies and haplotype associations (frequencies) between different alleles, like HLA-B and HLA-C, HLA-DRB1 and HLA-DQB1.

## Allele Code Lists

**Allele Code Lists: https://bioinformatics.bethematchclinical.org/hla-resources/allele-codes/allele-code-lists/**

On this page you can find links to lists with all current multiple allele codes. You can choose between two lists which differ in sorting: numerically and alphabetically. Examples of both are shown in figure 7.

| CODE | SUBTYPE | CODE | SUBTYPE |
|---|---|---|---|
| AB | 01/02 | AA | 01/02/03/05 |
| AC | 01/03 | AB | 01/02 |
| AD | 01/04 | AC | 01/03 |
| AE | 01/05 | AD | 01/04 |
| AG | 01/06 | AE | 01/05 |
| AH | 01/07 | AF | 01/09 |
| AJ | 01/08 | AG | 01/06 |
| AF | 01/09 | AH | 01/07 |
| JV | 01/10 | AJ | 01/08 |
| JZDV | 01/100 | AK | 01/13 |
| KVKC | 01/101 | AM | 01/14 |
| WBEB | 01/102 | AN | 03/06/11/12 |
| JJRT | 01/103 | AP | 02/04/07/11 |
| RZGB | 01/104 | AR | 01/03/06/10 |
| JECK | 01/105 | AS | 07/11 |

Figure 7: Beginning of the allele code lists. On the left, the numerically sorted list and on the right, the alphabetically sorted list.

## MAC Service UI (previously known as DNA Type Lookup Tool)

**Mac Service UI: https://hml.nmdp.org/MacUI/**

With this tool you can lookup which alleles are included in a multiple allele code and also which code should be designated to a group of alleles. In figure 8 you can see the user interface of this tool.

**To lookup a multiple allele code (MAC): Use the fields on the right side of the tool**

**STEP 1**: Type in or paste the allele, e.g. B*08:YETY, in the MAC designation look up box on top of the right fields.

**STEP 2**: Click on the 'Decode' or 'Expand' button. If you choose for decode, the MAC is just decoded with the locus and allele family provided. If you choose expand, then also the alleles within the MAC are checked for validity based on the IPD-IMGT/HLA database release that can be selected on the top of the left fields of the user interface. This means that it will also include alleles with more than 4 digits. The results will be shown in the decode result or expand result box depending on the function you have chosen.

NOTE: the tool does not show you any message when a MAC became deprecated or invalid. You can check

it by copying the decode result into the encode box and click on the Look Up button. You will then receive the message that the MAC designation contains an invalid allele meaning that the MAC will be deprecated or invalid.

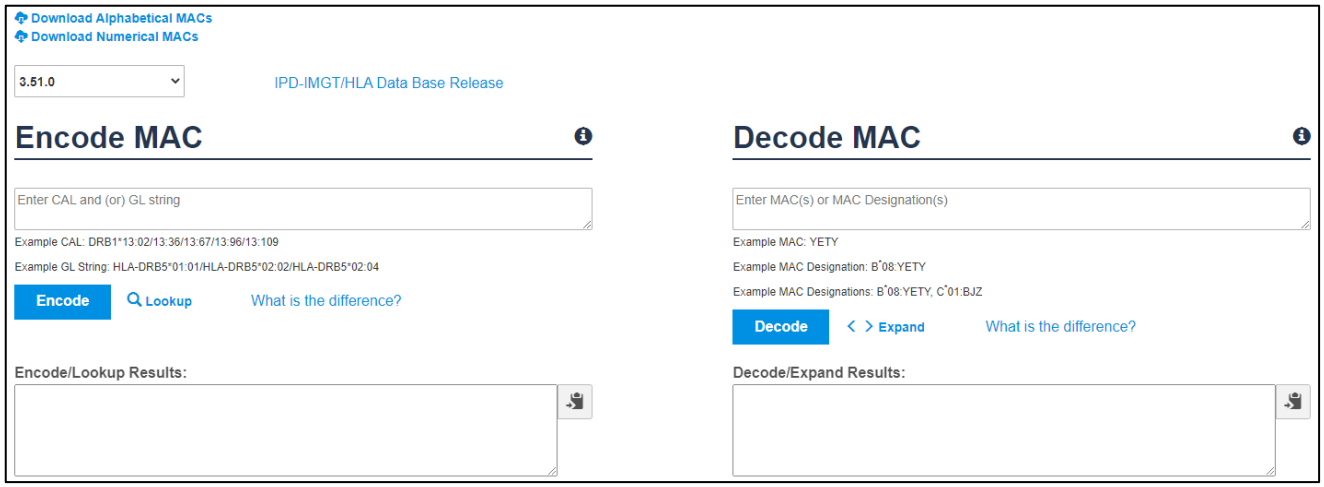


Figure 8: User interface of the MAC Service UI.

**To lookup a MAC for a list of alleles: Use the fields on the left side of the tool**

**STEP 1**: Type in or paste all alleles in the Encode look up input box at the left side of the tool.

**STEP 2**: Click on the 'Lookup' or 'Encode' button. Use Lookup when you just want to look if a MAC exists for your allele list. Use Encode when you also directly want to create a new MAC when no MAC is existing for your allele list.

## ZKRD

| Website address | http://optimatch.zkrd.de/services/LAnominfo/ |
|---|---|
| **What can I find here?** | This specific website from the ZKRD contains information on the following topic:<br>• ListHLA.net (alternative MAC/ DNA Type Lookup Tool)<br>This tool can help you to look-up MACs and can also show you information on for example allele frequencies and serological equivalents. |
| **Navigation on website** | Navigation is within the three tabs on the main page. The 'show help' button gives more explanation on the search results within each of the tabs. |

Figure 9 shows you the user interface of the ListHLA.net tool, which can be used as an alternative for the MAC Service UI from the NMDP. We will shortly describe how to use the tool. For more information on the interpretation of the results, we refer to the explanation that is shown when you click on the 'show help' button.

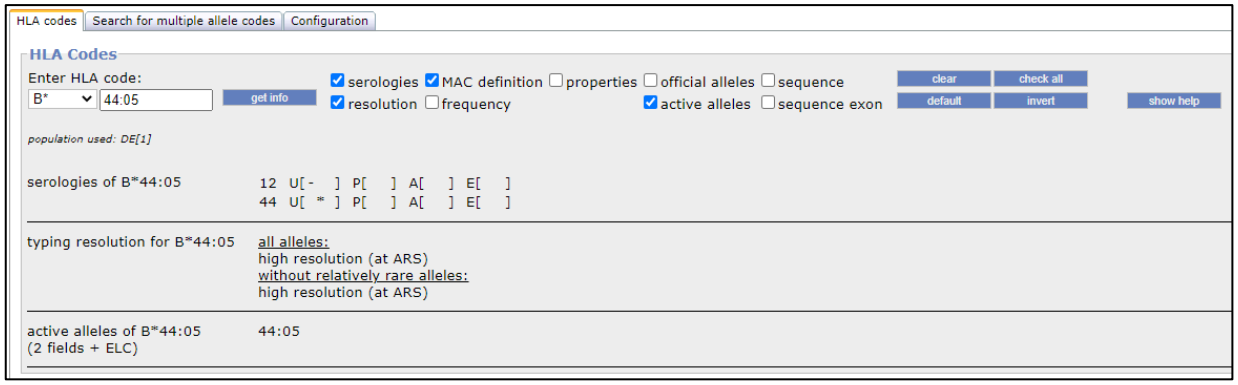



Figure 9: User interface of the ListHLA.net tool and the results for B*44:05 in the German population.

**HLA codes tab: To lookup a MAC**

Type in the MAC (e.g. AB) in the second field under 'Enter HLA code' and do not select any locus in the first field. Press enter, and you will see your result (in this example: multiple allele code definition AB=01/02).

**HLA codes tab: To lookup more information on alleles/antigens**

Select the correct locus and type in the name of the allele/antigen you would like to lookup. This can be a serological value (e.g. A10), high resolution allelic value (e.g. A*01:01:02), or a allelic value containing a MAC (e.g. A*01:AB). You can select on the right side which information you would like to retrieve. To get the information, click on the 'get info' button.

The frequencies of the active allele(s) are dependent on the population you choose in the third tab: configuration. You can either choose between the German (DE) or Polish (PL) population.

**Search for multiple allele codes tab**: **To lookup a MAC for two or more alleles**

Select the correct locus and type in two or more alleles in the second field (e.g. A*01:01 01:02).When you

click on ‘search’ you will retrieve valid MACs that include your alleles, but might contain additional alleles as well.

On the right side you can select the options ‘exact match’ and ‘show deprecated MACs’. When you select ‘exact match’ the results will be reduced to the MACs that contain only the given alleles. When you select ‘show deprecated MACs’, the results will include deprecated MACs besides the exact match results.

## Haplotype frequencies: HaploStats

| Website address | http://www.haplostats.org |
|---|---|
| **What can I find here?** | This website contains a haplotype tool based on the haplotype frequencies determined in the donor population from the NMDP/Be the Match (USA).<br>You can use this tool to estimate the likely haplotypes of your patient and in what kind of population these are most familiar.<br>You can also use this tool to find out the likely population were you can find a match when only e.g. HLA A, B and DRB1 are known in your donor list, by filling out the form with the HLA results of one of the potential matched donors. |
| **Navigation on website** | Navigation is based on filling out a form and retrieving your results after submission. |

**STEP 1**: Fill out the form on the website. A screenshot of the form is shown in figure 10.

- **Dataset**: Choose between NMDP full 2011 and NMDP high res 2007. Default is NMDP full 2011. The other dataset only includes haplotype frequency information based on high resolution HLA typing results from NMDP donors.
- **Population**: If you are not so familiar with haplotype frequencies, it is better to use the default settings for populations (your results will then include all populations). Otherwise you can select a specific population.
- **Haplotype Loci**: You can select how many loci you want to consider in your results. Default is 5 loci, HLA-A,B,C,DRB1,DQB1.

**HLA type**: Fill out the HLA results you know from your patient or from a potential matched donor.

Click on 'submit query' to retrieve your results.

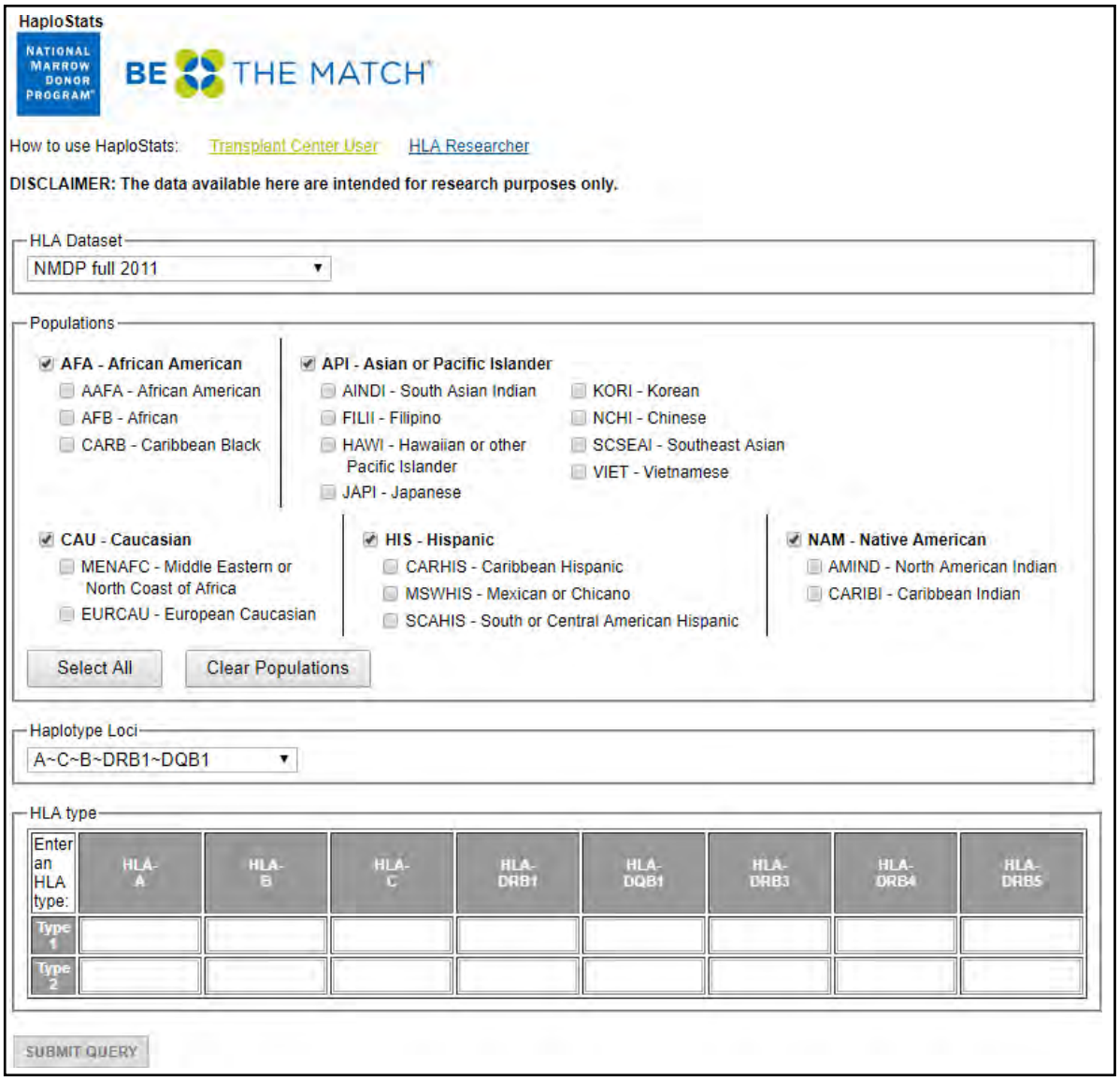


Figure 10: HaploStats search form on home page.

**STEP 2**: Results: Below in figure 11 you find a screenshot of an example of the collapsed results.

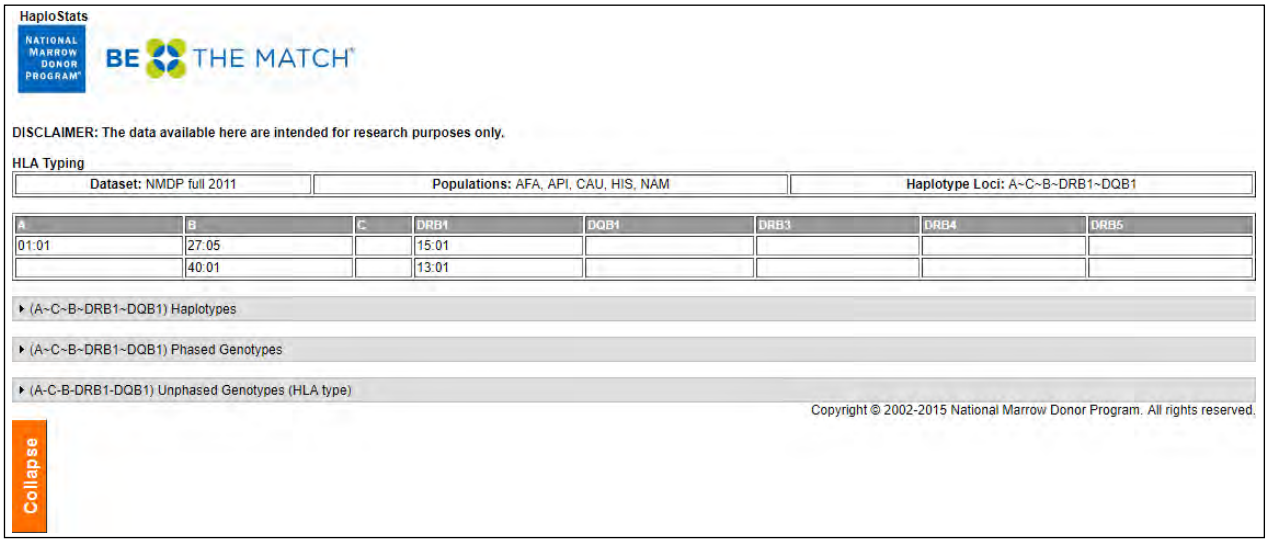
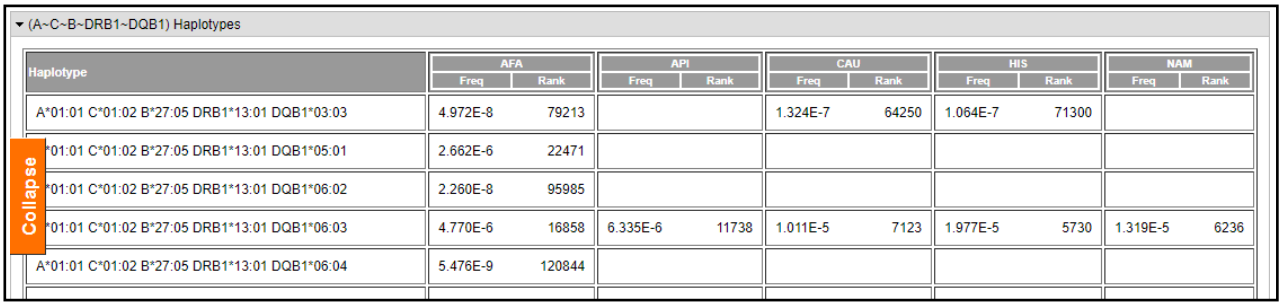


Figure 11: Collapsed results of a search in HaploStats.

At the top of the results you can find what you entered and selected in the form at the home page.

The actual results are shown at the collapsed bars:

**(A~C~B~DRB1~DQB1) Haplotypes**: Includes all possible haplotypes within the selected populations with their frequency and rank. A lower rank number means that this haplotype frequency is more likely.




| Haplotype | AFA | | API | | CAU | | HIS | | NAM | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Freq | Rank | Freq | Rank | Freq | Rank | Freq | Rank | Freq | Rank |
| A*01:01 C*01:02 B*27:05 DRB1*13:01 DQB1*03:03 | 4.972E-8 | 79213 | | | 1.324E-7 | 64250 | 1.064E-7 | 71300 | | |
| *01:01 C*01:02 B*27:05 DRB1*13:01 DQB1*05:01 | 2.662E-6 | 22471 | | | | | | | | |
| *01:01 C*01:02 B*27:05 DRB1*13:01 DQB1*06:02 | 2.260E-8 | 95985 | | | | | | | | |
| *01:01 C*01:02 B*27:05 DRB1*13:01 DQB1*06:03 | 4.770E-6 | 16858 | 6.335E-6 | 11738 | 1.011E-5 | 7123 | 1.977E-5 | 5730 | 1.319E-5 | 6236 |
| A*01:01 C*01:02 B*27:05 DRB1*13:01 DQB1*06:04 | 5.476E-9 | 120844 | | | | | | | | |

Figure 12: HaploStats results: All possible haplotypes within selected populations with frequency and rank.

**(A~C~B~DRB1~DQB1) Phased Genotypes:** These results (figure 13) show you the likely haplotype frequencies if the haplotypes are phased. This means that the HLA alleles shown are all located on the same chromosome.

- **The bar chart:** Indicates the relative (sum) frequency of individual genotype frequencies listed under each displayed population. The population with the highest sum frequency over all genotypes is used as the reference population when determining the scale for the overall bar graph display.
- **Population HLA type frequencies:** There are horizontal bar graphs displaying relative frequencies for the top 6 genotypes found within each of the populations requested. The vertical bar to the right of the horizontal bar graph represents the same information found in the larger Genotype frequency bar graph at the top of the Phased Genotypes results.
- **HLA typing resolution score:** Typing ambiguity score measures the content of ambiguity or uncertainty in the typing for a given population.

After these charts a list of haplotype pairs is displayed. There is a column for each population originally selected for inclusion in the results. The population frequency, and rank of each haplotype in the set of haplotype pairs is reported along with the frequency, rank and likelihood of the genotype they comprise being observed in the reference population.

Haplotype pairs are sorted within each population from highest to lowest frequency. Therefore, haplotype pairs do not line up across columns but are sorted independently within population columns.

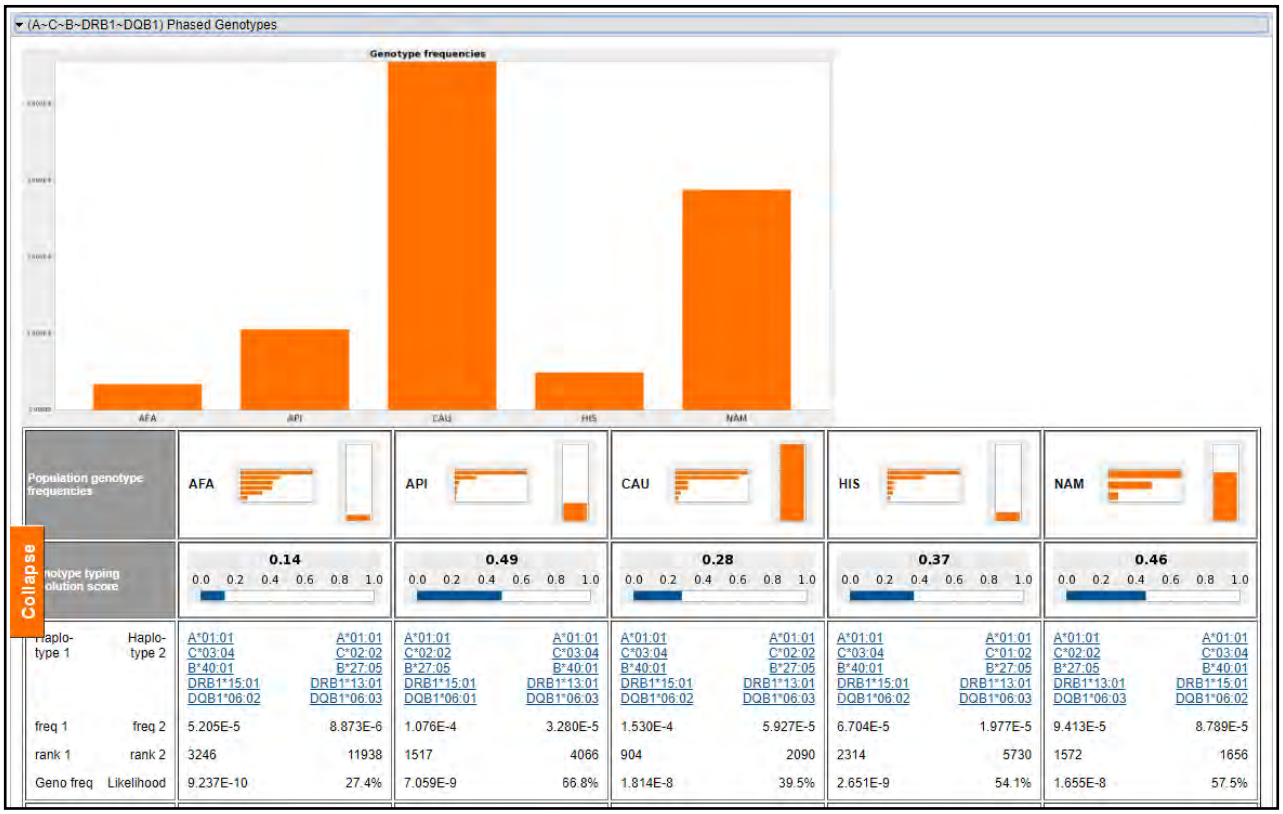



Figure 13: HaploStats results: Phased Genotypes.

You can also click on the haplotypes to retrieve a global HLA haplotype Map which shows the distribution of this haplotype within the world (figure 14). Only HLA-A, -B, and -DRB1 are considered in these haplotype maps.

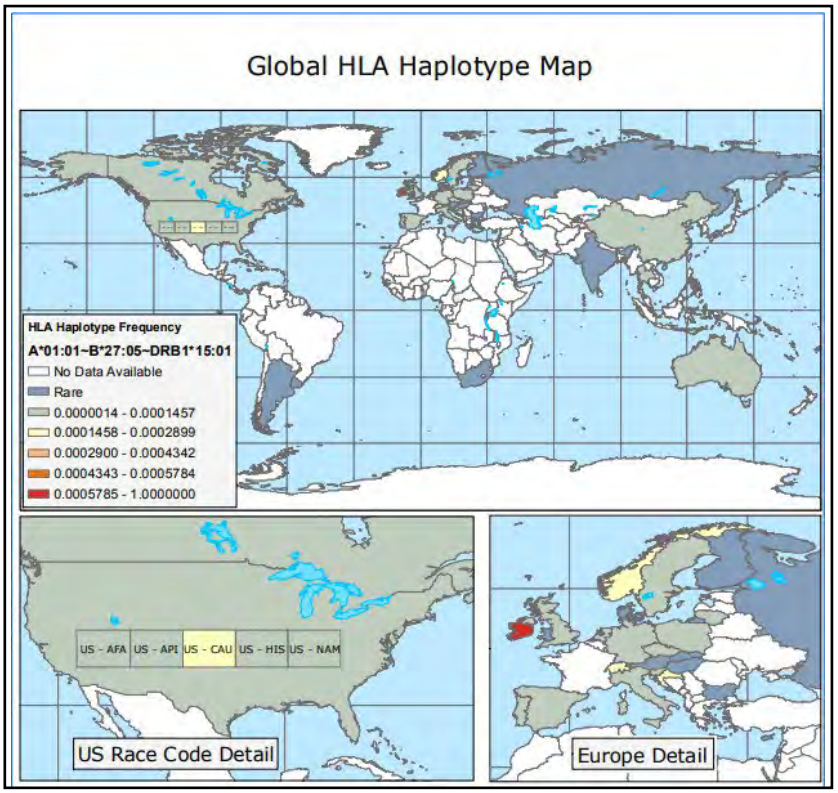



Figure 14: Haplotype frequency distribution.

**(A~C~B~DRB1~DQB1) Unphased Genotypes (HLA type):** This section contains information about the unphased genotypes imputed from the HLA typing entered. It is similar in layout to the Phased Genotypes section as it essentially contains aggregated information from this section. The difference between these two sections is that the Unphased Genotypes section does not include any haplotype or phase information. So these are the genotypes without regard to which one of the pair of chromosomes holds the HLA alleles (figure 15).

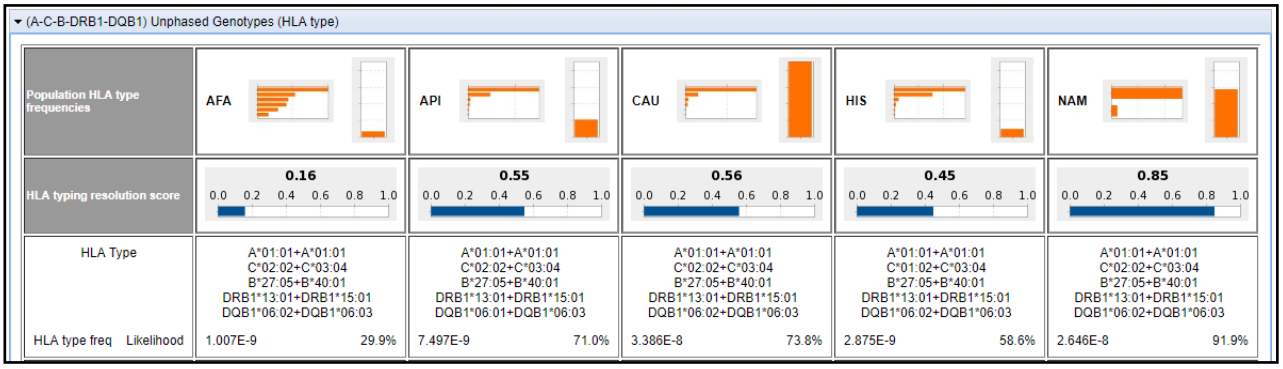


Figure 15: HaploStats results: Unphased Genotypes.

For some more details or background information you can also look into the HaploStats manual: **https://bioinformatics.bethematchclinical.org/workarea/downloadasset.aspx?id=6339**

## Allele Frequencies

| Website address | http://www.allelefrequencies.net/ |
|---|---|
| **What can I find here?** | This website from the Allele Frequency Net Database (AFND) provides allele frequency information within different countries for e.g. HLA alleles, but also other polymorphic areas in the human genome. You can also find here information on rare HLA alleles and KIR genes/alleles. |
| **Navigation on website** | With the navigation bar at the top left side, you can go to HLA and then choose a submenu.<br>Other interesting subjects are Populations, Rare alleles and KIR. |

### Allele Frequency Search (HLA Allele Freq (Classical))

With this tool you can identify the allele frequencies of the more classical HLA genes (HLA-A,B,C,DRB1,DQB1,DPB1,DPA1,DQA1) within different countries or subpopulations of countries. Allele frequencies of other HLA genes can be searched with the non-classical tool.

**STEP 1:** Fill out the form as shown in figure 16. If you just want to see the allele frequencies of 1 specific allele, enter then the allele name in the starting and ending allele box; make sure you also provide the gene, so A*01:01:01 and not just 01:01:01, even though you already specified the locus.

If you want to see all allele frequencies of a certain population, you should leave the starting and ending allele boxes empty and specify the population. It is also possible to look only in populations with a certain ethnic origin.

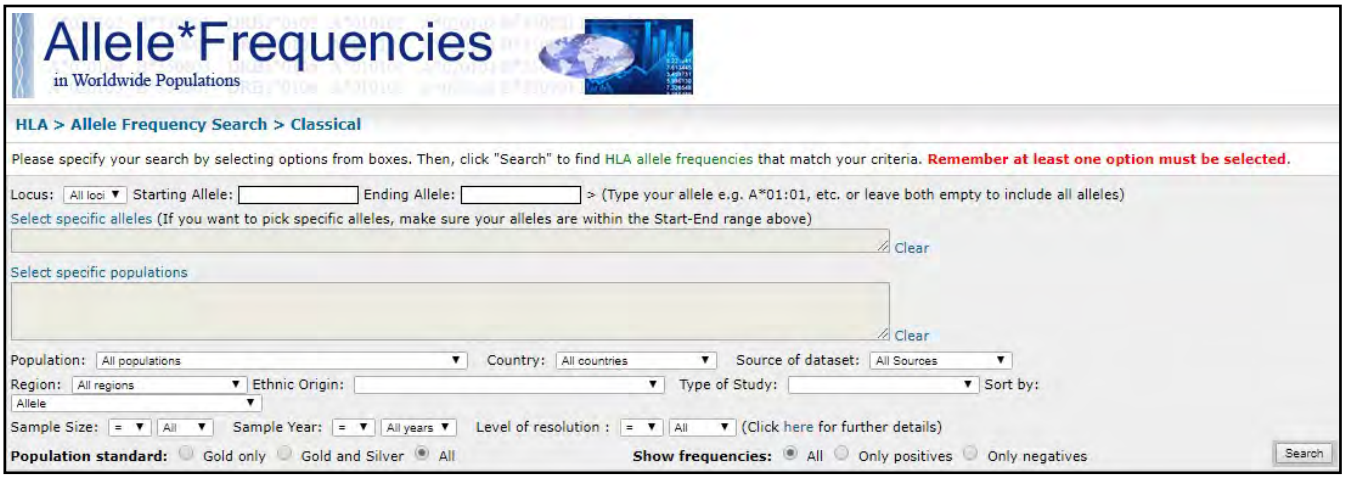


Figure 16: Allele frequency search for classical HLA genes.

**STEP 2:** Results: the screenshot in figure 17 shows you a part of the results for A*01:01:01. It includes the population name, percentage of individuals that carry the allele, the allele frequency, the sample size of the population in which the frequency was determined. It also includes a link to the allele information in the IMGT/HLA database.

| Line | Allele | Population | % of individuals that have the allele | Allele Frequency (in_decimals) | Sample Size | IMGT/HLA[1] Database | Distribution[2] | Haplotype[3] Association | Notes[a] |
|---|---|---|---|---|---|---|---|---|---|
| 1 | A*01:01:01 | Bulgaria | | 0.0730 | 55 | See | | | |
| 2 | A*01:01:01 | Cape Verde Northwestern Islands | | 0.0480 | 62 | See | | | |
| 3 | A*01:01:01 | Cape Verde Southeastern Islands | | 0.0480 | 62 | See | | | |
| 4 | A*01:01:01 | China North Han | | 0.0710 | 105 | See | | | |
| 5 | A*01:01:01 | China Tibet Region Tibetan | | 0.0220 | 158 | See | | | |
| 6 | A*01:01:01 | England Blood Donors of Mixed Ethnicity | 37.4 | 0.206200 | 519 | See | | | |
| 7 | A*01:01:01 | Guinea Bissau | | 0.0460 | 65 | See | | | |
| 8 | A*01:01:01 | India Andhra Pradesh Telugu Speaking | 28.5 | 0.147850 | 186 | See | | | |
| 9 | A*01:01:01 | Iran Baloch | | 0.0170 | 100 | See | | | |
| 10 | A*01:01:01 | Japan Okinawa Ryukyuan | | 0.0040 | 143 | See | | | |

Figure 17: Results of allele frequency search for A*01:01:01.

**STEP 3:** When you click on the population name, you will see more information like the test date and if the results were published.

**STEP 4:** When you click on the Distribution icon, you will see the global allele frequency distribution in a world map (figure 18) and also in bar charts per geographical area. The allele frequency is represented by coloured dots with blue on the left for the lower allele frequencies and going to the right the allele frequencies increase.

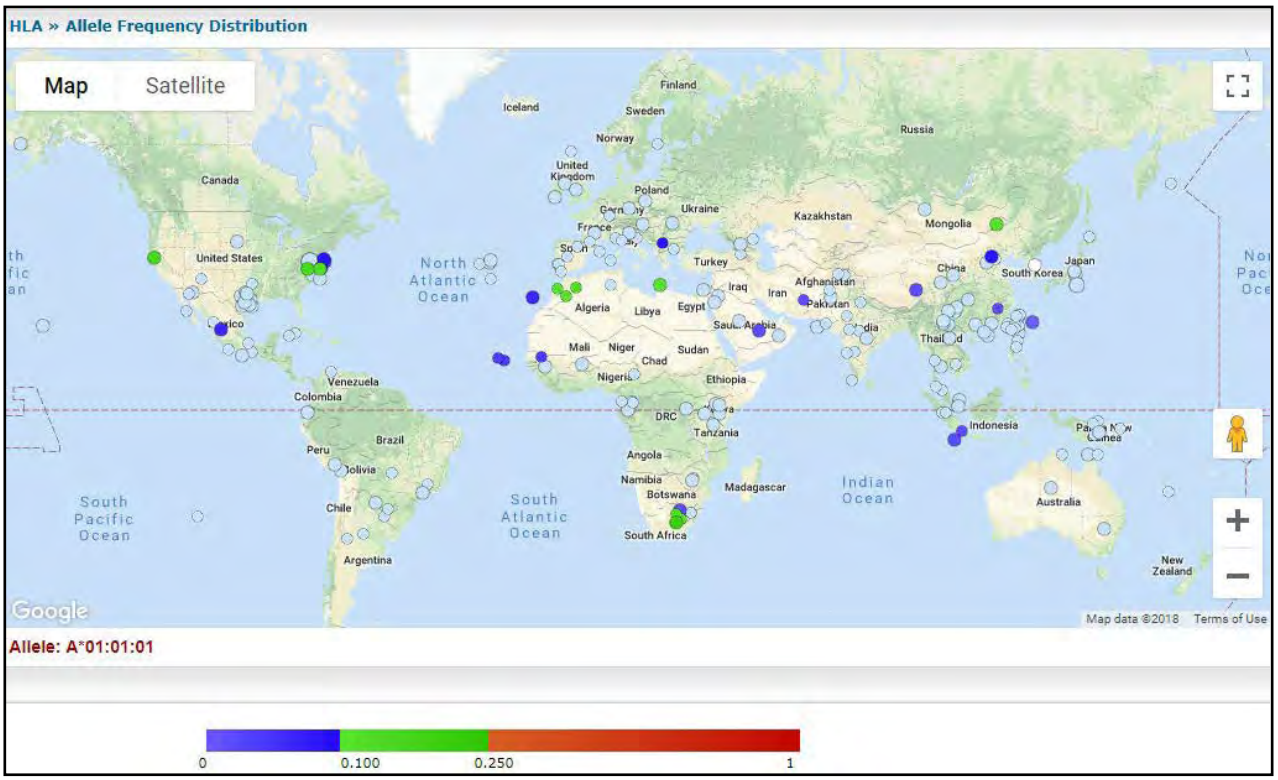



Figure 18: Global allele frequency distribution over the world.

## Haplotype Frequency Search

With this tool you can identify the haplotype frequencies of the more classical HLA genes (HLA-A,B,C,DRB1,DQB1,DPB1,DPA1,DQA1) within different countries or subpopulations of countries.

**STEP 1:** Fill out the haplotype frequency search form with the haplotype of your interest. You can also retrieve all haplotypes with their frequencies within a certain population when you leave the fields of the haplotype empty (figure 19).

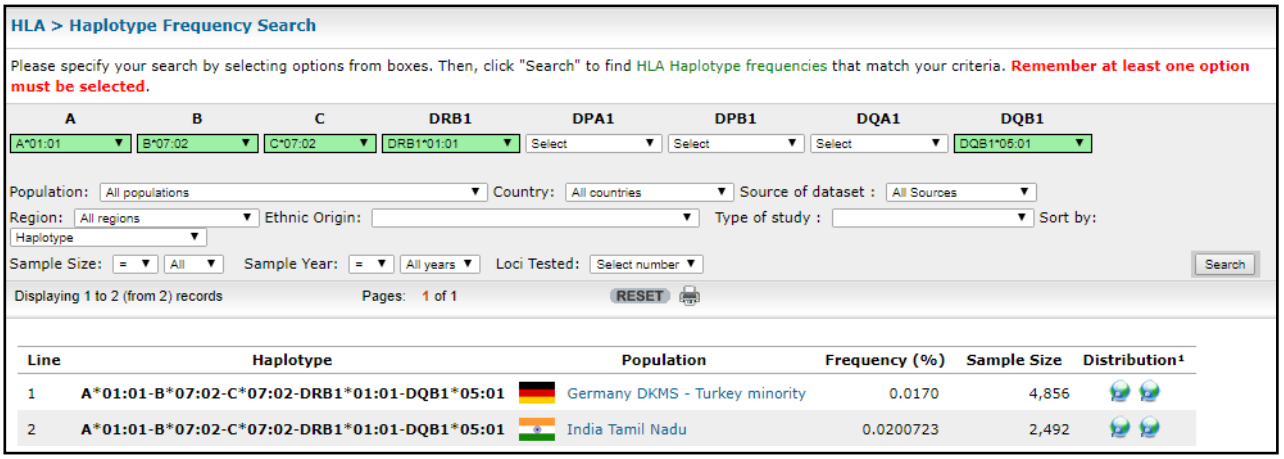


Figure 19: Haplotype frequency search.

## Allele Frequency Distribution

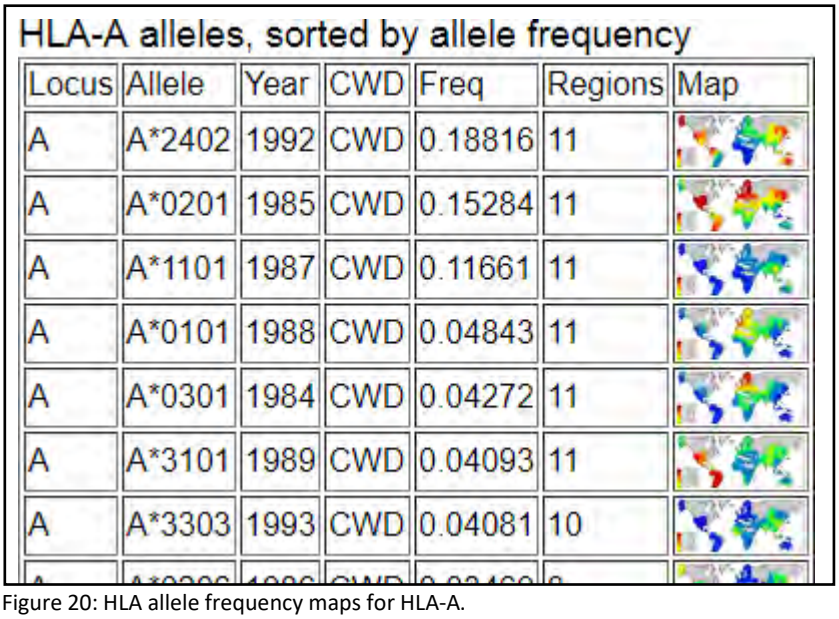
| Website address | http://pypop.org/popdata/ |
|---|---|
| **What can I find here?** | This website provides allele frequency maps and a list of all the populations (and publications) used to create these maps. The maps are available for HLA-A,B,C,DRB1,DQA1,DQB1,DPA1 and DPB1. All information is based on a publication of Solberg et al(2008): *Balancing selection and heterogeneity across the classical human leukocyte antigen loci: A meta-analytic review of 497 population studies.* |
| **Navigation on website** | On the main page you can find an index with the links to the information. The HLA allele frequency maps and the index of population datasets are the most useful links for search coordinators. |

### HLA Allele Frequency Maps

These maps show the global distribution of an HLA allele based on allele frequencies determined in previous population studies.

**STEP 1:** On the main page, click on the HLA locus from the allele you would like to get the allele frequency information from.

**STEP 2:** When you click on HLA-A in the first step you will see the table as in figure 20.



HLA-A alleles, sorted by allele frequency

| Locus | Allele | Year | CWD | Freq | Regions | Map |
|---|---|---|---|---|---|---|
| A | A*2402 | 1992 | CWD | 0.18816 | 11 | |
| A | A*0201 | 1985 | CWD | 0.15284 | 11 | |
| A | A*1101 | 1987 | CWD | 0.11661 | 11 | |
| A | A*0101 | 1988 | CWD | 0.04843 | 11 | |
| A | A*0301 | 1984 | CWD | 0.04272 | 11 | |
| A | A*3101 | 1989 | CWD | 0.04093 | 11 | |
| A | A*3303 | 1993 | CWD | 0.04081 | 10 | |

Figure 20: HLA allele frequency maps for HLA-A.

You can change the view of this table at the top of the page. The table can be sorted either on allele frequency (default) or on allele name.

Further explanation of the columns in the table:

- **Year** is the year the allele was first described in the literature.
- **CWD** indicates that the allele is considered Common and Well-Documented by Cano et. al. (2007).
- **Freq** is the overall average frequency, across all population samples included in the Solberg et. al.

(2008) publication.

- **Regions** is the number of world regions the allele appears in.
- The **Map** link provides a geographical interpolation of allele frequency, using only non-migrant populations (maps are not available for a few alleles because of this).

NOTE: The maps should be considered crude approximations of regional patterns. Maps are also not available when the allele frequency is nearly zero.

**STEP 3:** When you click on the map link, you see a world map as in figure 21 for HLA-A*02:01. The colours represent the allele frequencies in a region with dark red for a high frequency and the dark blue for very low frequencies.

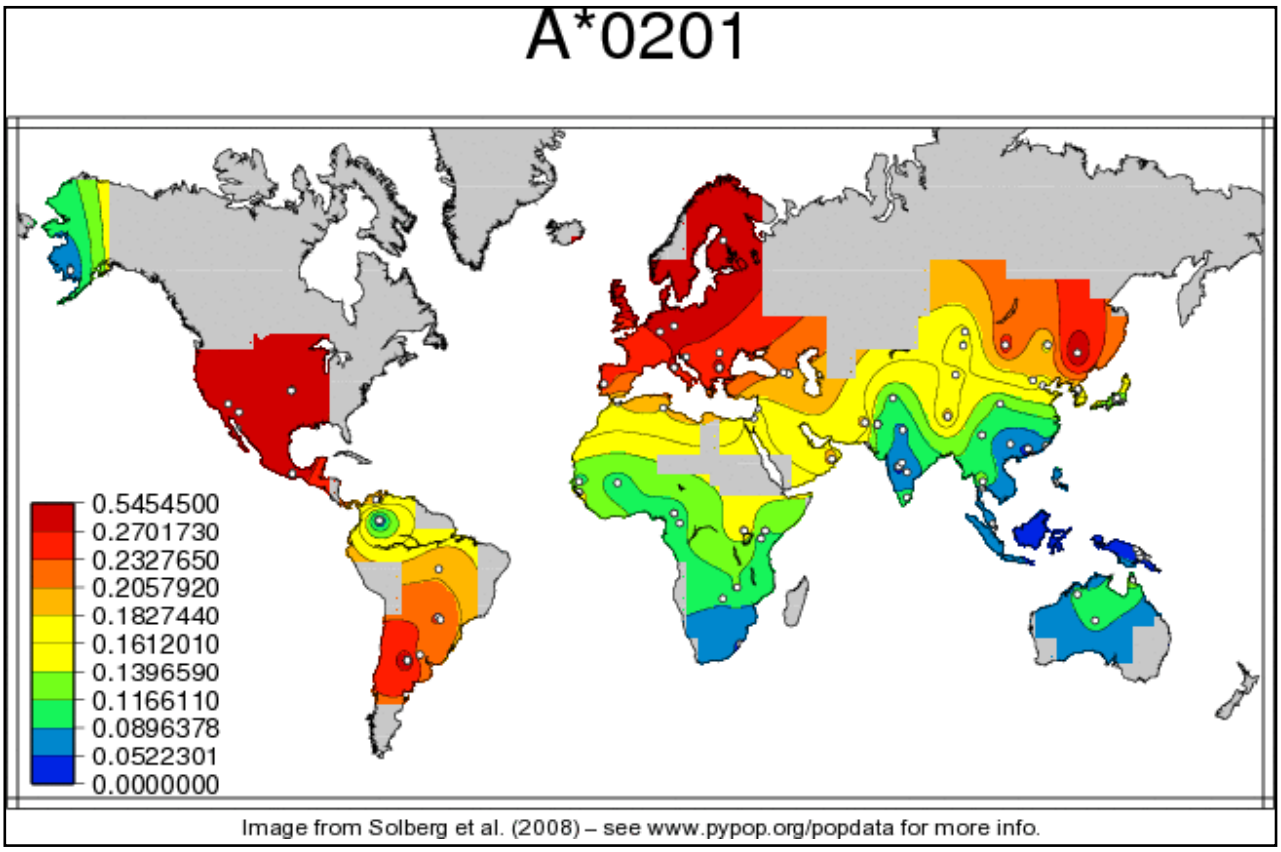



Figure 21: HLA-A*02:01 frequency distribution over the world.

## Index of population datasets

This function shows you information about the included populations, where and when they were published and the sample size. It is sorted by region followed by population name.

| region | popname | First author, year | A | C | B | DRB1 | DQA1 | DQB1 | DPA1 | DPB1 |
|---|---|---|---|---|---|---|---|---|---|---|
| EUR | Austria_1993 | Pickl 1993 | | | | | | | | 980 |
| EUR | Basques_1998 | Comas 1998 | | | | | | | 200 | 196 |
| EUR | Basques_2003 | Perez-Miranda 2003 | | | | | 224 | | | |
| EUR | Basques_2004 | Perez-Miranda 2004 | | | | | | | 232 | 192 |
| EUR | Breton_1995 | Raguenes 1995 | | | | | | | | 300 |
| EUR | British_1992 | Doherty 1992 | | | | | 354 | 354 | | |
| EUR | British_1994 | Sage 1994 | | | | | | | | 374 |
| EUR | British_1994b | Wu 1994 | | | | | 118 | 100 | 122 | 124 |
| EUR | Bulgarians_2002 | Ivanova 2002 | 110 | | 110 | 110 | | | | |
| EUR | Cabuerniges_2003 | Sanchez Velasco 2003 | | | | 190 | 190 | | | |

Figure 22: First part of table with populations.

Further explanation of the columns:

- The First author, year column links to the PubMed record for the published work.
- Last 8 columns indicate the 2n sample size for each of the classical HLA loci studied. Clicking on the number will display the PyPop-formatted datafile for that population and locus.

## Statistics Search & Match Service

| Website address | https://statistics.wmda.info/ |
|---|---|
| **What can I find here?** | This website shows all organisations that list donors and/or cord blood units in WMDA Search & Match Service and their numbers, accreditation status and date of last update.<br>You can export the results in different file formats. |
| **Navigation on website** | On the main page of wmda.info, you can find somewhat below a red block with Statistics Search & Match Service. When you click on this, a new tab will open with the table with information.<br>On the statistics page you can click on trend and density to get some additional information. |

The database of WMDA Search & Match Service contains many donors and cord blood units (CBU). On top of the main page you can find the general statistics of the whole database, showing:

- Total number of donors
- Total number of CBUs
- Total records (donors + CBUs)
- Number of organisations listing and number of countries listing.

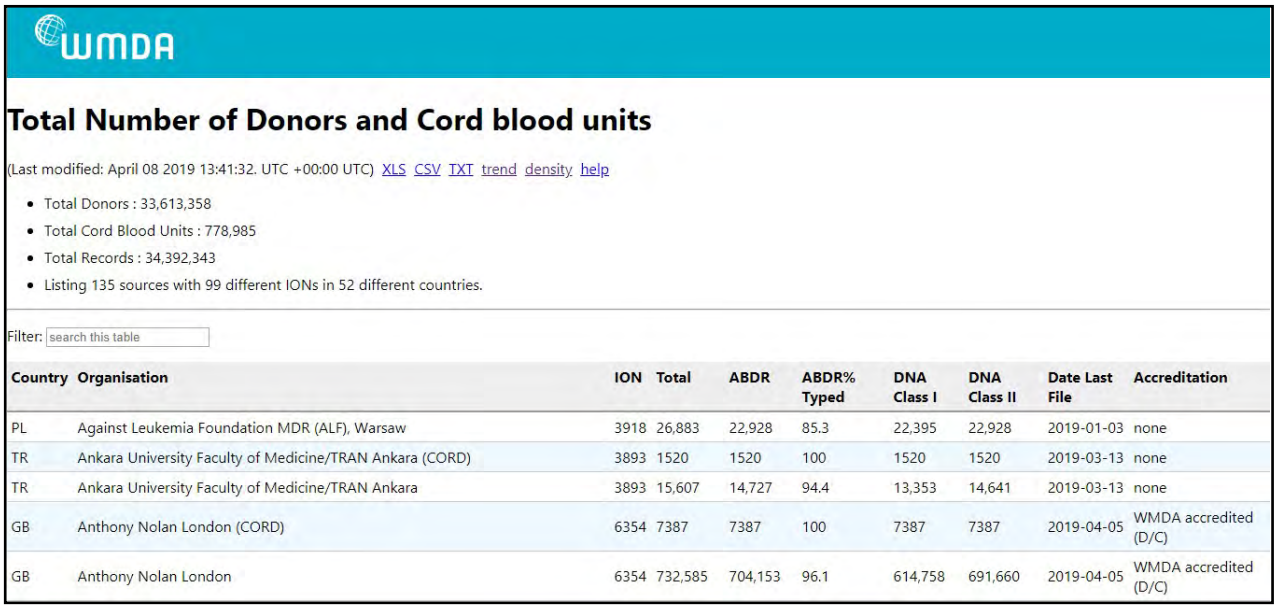
In the table, the numbers are specified for each listing organisation including the following information:

- Country (ISO code), organisation name, ION
- Total number of donors/CBUs for each organisation (Total)
- How many donors/CBUs have been genotyped for HLA A,B,DR and the percentage
- How many donors/CBUs have been genotyped for DNA class I and class II HLA genes
- Date when the inventory was last updated (Date Last File)
- WMDA accreditation status (Accreditation)

The first part of the list is shown in figure 23. You can also use the filter to search for specific definition/words and ascending/descending sort the data by clicking on a column header. The data can be exported in three different file formats: XLS, CSV, and TXT on the top of the page.

In your search for a potential matched donor or CBU, especially the following data is important:

- The organisation names shown in the table are sometimes the same for the donor registry and cord blood bank. Please note that for the cord blood bank, the suffix (CORD) is added to the name.
- The table only shows the WMDA accreditation status, which can be accredited, qualified or empty if an organisation is not WMDA accredited or qualified. Please note, that an organisation can be accredited/qualified for their donor registry (D), cord blood banks (C), or for both (D/C). If an organisation has both donors and cords, but is only accredited/qualified for donors only, this status will also show up in the row from the cord blood bank from this organisation.
- If you would like to know other accreditation statuses, like FACT or AABB, please check the following website: https://share.wmda.info/display/WMDAREG/Database
- The 'Date Last File' can be useful during the search. If you see in the table that the organisation has not updated their inventory very recently, it might be worth to send a preliminary search request to the organisation directly as donors/CBUs might be missing in Search & Match Service.



## Total Number of Donors and Cord blood units

(Last modified: April 08 2019 13:41:32. UTC +00:00 UTC) XLS CSV TXT trend density help

- Total Donors : 33,613,358
- Total Cord Blood Units : 778,985
- Total Records : 34,392,343
- Listing 135 sources with 99 different IONs in 52 different countries.

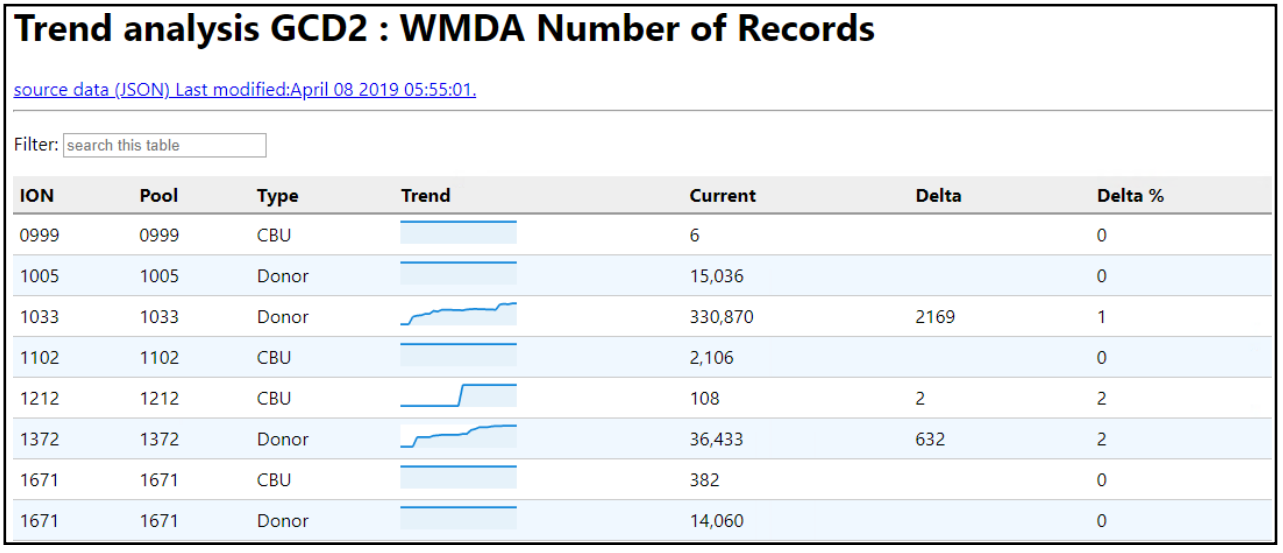
Filter: search this table

| Country | Organisation | ION | Total | ABDR | ABDR% Typed | DNA Class I | DNA Class II | Date Last File | Accreditation |
|---|---|---|---|---|---|---|---|---|---|
| PL | Against Leukemia Foundation MDR (ALF), Warsaw | 3918 | 26,883 | 22,928 | 85.3 | 22,395 | 22,928 | 2019-01-03 | none |
| TR | Ankara University Faculty of Medicine/TRAN Ankara (CORD) | 3893 | 1520 | 1520 | 100 | 1520 | 1520 | 2019-03-13 | none |
| TR | Ankara University Faculty of Medicine/TRAN Ankara | 3893 | 15,607 | 14,727 | 94.4 | 13,353 | 14,641 | 2019-03-13 | none |
| GB | Anthony Nolan London (CORD) | 6354 | 7387 | 7387 | 100 | 7387 | 7387 | 2019-04-05 | WMDA accredited (D/C) |
| GB | Anthony Nolan London | 6354 | 732,585 | 704,153 | 96.1 | 614,758 | 691,660 | 2019-04-05 | WMDA accredited (D/C) |

Figure 23: Table with statistics from the WMDA Search & Match Service database.

### Trend information

When you click on 'trend' on the main page, you will see the trend analysis of all organisations. It shows (figure 24) a small graph with the trend, based on the number of records send by the organisations.



## Trend analysis GCD2 : WMDA Number of Records

source data (JSON) Last modified:April 08 2019 05:55:01.

Filter: search this table

| ION | Pool | Type | Trend | Current | Delta | Delta % |
|---|---|---|---|---|---|---|
| 0999 | 0999 | CBU | | 6 | | 0 |
| 1005 | 1005 | Donor | | 15,036 | | 0 |
| 1033 | 1033 | Donor | | 330,870 | 2169 | 1 |
| 1102 | 1102 | CBU | | 2,106 | | 0 |
| 1212 | 1212 | CBU | | 108 | 2 | 2 |
| 1372 | 1372 | Donor | | 36,433 | 632 | 2 |
| 1671 | 1671 | CBU | | 382 | | 0 |
| 1671 | 1671 | Donor | | 14,060 | | 0 |

Figure 24: Trend analysis of WMDA Search & Match Service database.

If an organisation didn't update their data in the last month, you will see a flat line. If an organisation regularly updates their data, you can see a trend, including the current number of records and the difference between the lowest and highest data point in absolute numbers and percentages.

**Density information**

If you click on ‘density’ on the main page, you will see the density information of all fields organisation can send for their records of the last 90 days. These densities are determined once per week and show summary data of the whole database.

You can select the results from donors, CBUs, or donors and CBUs together. In figure 25 you can see a part of the density output from donors in the default format.

The results can be shown in absolute numbers (/1000) or in percentages (default) by clicking on ‘/1000’ or ‘%’ at the cell values field.

The fields send by organisations can be specific for donors or CBUs, but can also be present in records for both, like date of birth. At ‘Fieldtypes’, you can select which fields you would like to see in the density map.

You can also change the appearance of the heat map at ‘Format’. When you select ‘Square’ the fields become squares instead of rectangular (Default). The colour pattern will change when you select ‘Sequential’ or ‘5 class diverge’.

All data can be downloaded in csv format by clicking on the ‘data-large.csv’ button. This file includes all raw data and disregards any of your previous selections (like donor only).

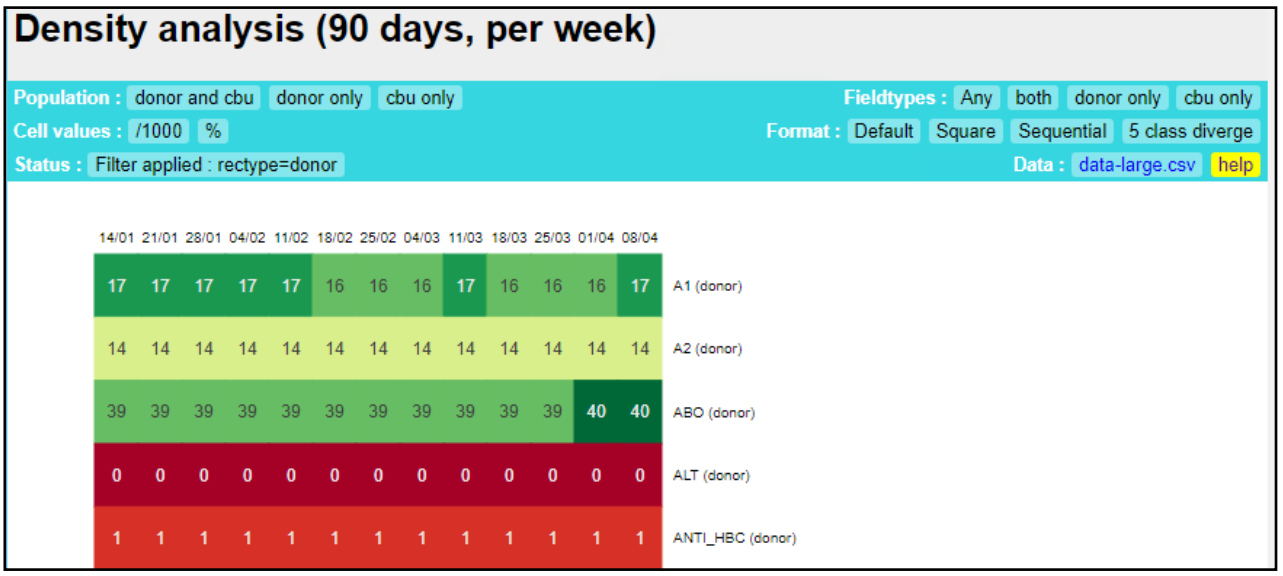



Figure 25: Density results of all fields that organisations can send for their records. Results are shown for population donor only and in percentages. This example shows that a value for blood group is present for 39-40% of the donors in the database.

## Quick access to website addresses based on order in search tool guide

| NAME TOOL | USEFUL FOR | WEBSITE ADDRESS |
|---|---|---|
| HLA Nomenclature | Information on HLA nomenclature, e.g. valid and invalid alleles, G and P groups, serologically defined HLA antigens. | http://hla.alleles.org/nomenclature/index.html |
| IPD IMGT/HLA database | | https://www.ebi.ac.uk/ipd/imgt/hla/ |
| Alignment tools: Align and BLAST | Aligning a specific sequence to a reference HLA allele sequence. | https://www.ebi.ac.uk/ipd/imgt/hla/align.html |
| Alignment tools: BLAST | Aligning a nucleotide sequence or a protein sequence to a database of known sequences. | https://www.ebi.ac.uk/Tools/services/web_ncbiblast/ |
| HLA Dictionary | Information on HLA alleles. Useful for identifying potential stem cell donors who were typed by either serology or DNA-based methods. | https://www.ebi.ac.uk/ipd/imgt/hla/alleles/dictionary/ |
| Ambiguous Allele Combinations | List of all alleles that are identical over exons 2+3 for HLA class I and all alleles that are identical over only exon 2 for HLA class II. | https://www.ebi.ac.uk/ipd/imgt/hla/ambiguity/help/ |
| DPB1 T-Cell Epitope Algorithms | Calculator to predict permissive and non-permissive DPB1 mismatched between patient and donor. | https://www.ebi.ac.uk/ipd/imgt/hla/matching/ |
| Tools | List of tools; e.g. HLA allele ethnicity tool to lookup in which ethnicity an allele was first identified. | https://www.ebi.ac.uk/ipd/imgt/hla/about/tools/ |
| Releases | Quarterly reports of new, modified, and deleted sequences. | https://www.ebi.ac.uk/ipd/imgt/hla/release/ |
| Common and Well-Documented Alleles | This catalogue shows if an allele is common and well-documented or rare. | https://www.ihiw18.org/component-immunogenetics/download-common-and-well-documented-alleles-3-0/ |
| Be the Match/NMDP | | https://bioinformatics.bethematchclinical.org/ |
| Haplotype Frequencies | Allele/haplotype association frequencies for various race/ethnicity within USA population. | https://bioinformatics.bethematchclinical.org/hla-resources/haplotype-frequencies/ |
| Allele Code Lists | List of all current multiple allele codes (MACs). | https://bioinformatics.bethematchclinical.org/hla-resources/allele-codes/allele-code-lists/ |

| | | | |
|---|---|---|---|
| | MAC Service UI (DNA Type Lookup Tool) | Lookup tool for MACs: which alleles are included in a MAC and also which code should be designated to a group of alleles and request new MACs. | https://hml.nmdp.org/MacUI/ |

| | | | |
|---|---|---|---|
| ZKRD | | | |
| | ListHLA.net (DNA Type Lookup Tool) | Lookup tool for MACs: which alleles are included in a MAC and which code should be designated to a group of alleles.<br>Also some additional allele information, like allele frequency. | http://optimatch.zkrd.de/services/HLAnominfo/ |
| Haplotype Frequencies: HaploStats | | Haplotype tool (based on USA population) to estimate likely haplotypes of your patient, or identify likely population for finding a matched donor. | http://www.haplostats.org |
| Allele Frequencies | | | http://www.allelefrequencies.net/ |
| | Allele Frequency Search | Identify the allele frequencies of the more classical HLA genes (HLA-A,B,C,DRB1,DQB1,DPB1, DPA1,DQA1) within different countries or subpopulations of countries. | http://www.allelefrequencies.net/hla6006a.asp |
| | Haplotype Frequency Search | Identify the haplotype frequencies of the more classical HLA genes (HLA-A,B,C,DRB1,DQB1,DPB1, DPA1,DQA1) within different countries or subpopulations of countries. | http://www.allelefrequencies.net/hla6003a.asp |
| Allele Frequency Distribution | | | http://pypop.org/popdata/ |
| | HLA Allele Frequency Maps | Global distribution of an HLA allele based on allele frequencies shown as heat maps. | http://pypop.org/popdata/ |
| | Index of population datasets | Lists information on the included populations, where and when they were published and the sample size. | http://pypop.org/popdata/ |

## Decision tree to search tools/web addresses based on topics

| TOPIC | | | WEBSITE ADDRESS | PAGE |
|---|---|---|---|---|
| **ALLELE INFORMATION** | | | | |
| | FREQUENCIES | **Allele frequencies search**<br>*Identify the allele frequencies of the more classical HLA genes (HLA-A,B,C,DRB1,DQB1,DPB1, DPA1,DQA1) within different countries/subpopulations of countries* | http://www.allelefrequencies.net/hla6006a.asp | 24 |
| | | **Common and Well-Documented alleles**<br>*List of common and well-documented, and rare HLA alleles* | https://www.ihiw18.org/component-immunogenetics/download-common-and-well-documented-alleles-3-0/ | 12 |
| | | **Allele frequencies in ListHLA.net**<br>*Lookup tool for alleles and MACs; results can include allele frequencies* | http://optimatch.zkrd.de/services/HLAnominfo/ | 17 |
| | | **Allele frequencies (and haplotypes) in US population**<br>*Tables per locus with allele frequencies in US population (per ethnicity)* | https://bioinformatics.bethematchclinical.org/hla-resources/haplotype-frequencies/high-resolution-hla-alleles-and-haplotypes-in-the-us-population/ | 15 |
| | | **Allele frequencies and global distribution maps**<br>*Overall average frequencies across all populations* | http://pypop.org/popdata/ | 27 |
| | GLOBAL DISTRIBUTION | **Global distribution maps**<br>*Heatmaps of distribution of HLA alleles over the world* | http://pypop.org/popdata/ | 27 |
| | ALLELE DESCRIPTION | **Alleles/Allelic query form**<br>*Description and discovery information of an HLA allele, including sequence, discovery population, discovery date.* | https://www.ebi.ac.uk/ipd/imgt/hla/allele.html | 9 |
| | | **HLA Dictionary**<br>*Most probable serologic equivalent of alleles + links to allele reports* | https://www.ebi.ac.uk/ipd/imgt/hla/alleles/dictionary/ | 7 |
| | VALID/ INVALID ALLELES AND GROUPS | **Valid alleles**<br>*List of all valid HLA alleles separate for class I and class II alleles* | http://hla.alleles.org/alleles/class1.html<br>http://hla.alleles.org/alleles/class2.html | 5 |
| | | **Deleted alleles**<br>*List of all deleted HLA alleles with reason of deletion* | http://hla.alleles.org/alleles/deleted.html | 5 |
| | | **Null and alternative expressed HLA alleles**<br>*List of Null alleles (suffix 'N') and alternatively expressed alleles ( 'L', 'S', 'C', 'A' or 'Q')* | http://hla.alleles.org/alleles/nulls.html | 5 |
| | | **P groups**<br>*List of P Codes for HLA alleles having the same antigen binding domains* | http://hla.alleles.org/alleles/p_groups.html | 5 |
| | | **G groups**<br>*List of G codes for HLA alleles with identical nucleotide sequences across the exons encoding the peptide binding domains* | http://hla.alleles.org/alleles/g_groups.html | 5 |

| | | | | |
|---|---|---|---|---|
| | | **Ambiguous Allele Combinations**<br>*List of all alleles identical over exons 2+3 for HLA class I and all alleles identical over only exon 2 for HLA class II* | https://www.ebi.ac.uk/ipd/imgt/hla/ambiguity/help/ | 10 |
| | | **Releases**<br>*Quarterly reports of new, modified, and deleted sequences/alleles* | https://www.ebi.ac.uk/ipd/imgt/hla/release/ | 11 |
| | MULTIPLE ALLELE CODES (MACS) | **MAC Service UI**<br>*Lookup tool for MAC codes, translation of MACs, request new MAC* | https://hml.nmdp.org/MacUI | 15 |
| | | **Allele code list**<br>*List of all MACs* | https://bioinformatics.bethematchclinical.org/hla-resources/allele-codes/allele-code-lists/ | 15 |
| | | **ListHLA.net**<br>*Lookup tool for MAC codes and translation of MACs + additional info on e.g. allele frequencies* | http://optimatch.zkrd.de/services/HLAnominfo/ | 17 |
| | SEROLOGICAL HLA ANTIGENS | **HLA Dictionary**<br>*Most probable serologic equivalent of alleles* | https://www.ebi.ac.uk/ipd/imgt/hla/alleles/dictionary/ | 7 |
| | | **HLA Antigens**<br>*List of all serologically defined HLA antigens*<br>*List of broad, splits and associated HLA antigens (2e link)* | http://hla.alleles.org/antigens/recognised_serology.html<br>http://hla.alleles.org/antigens/broads_splits.html | 5 |
| | ALIGNMENTS | **BLAST**<br>*Aligning nucleotide sequence or protein sequence to a database of known sequences* | https://www.ebi.ac.uk/Tools/services/web_ncbiblast/ | 7 |
| | | **Align**<br>*Aligning a specific sequence to a reference HLA allele sequence* | https://www.ebi.ac.uk/ipd/imgt/hla/align.html | 6 |
| **HAPLOTYPE INFORMATION** | | **Haplotype frequency tables**<br>*Tables with allele/haplotype associations frequencies for various race/ethnicity within USA population* | https://bioinformatics.bethematchclinical.org/hla-resources/haplotype-frequencies | 15 |
| | | **Haplostats**<br>*Haplotype tool (based on USA population) to estimate likely haplotypes of patient, or find likely population for finding a matched donor* | http://www.haplostats.org | 19 |
| | | **Haplotype frequencies**<br>*Identify haplotype frequencies of the more classical HLA genes (HLA-A,B,C,DRB1,DQB1,DPB1, DPA1,DQA1) within different countries/subpopulations of countries.* | http://www.allelefrequencies.net/hla6003a.asp | 25 |
| **ETHNICITY** | | **Ethnicity tool**<br>*Lookup tool in which ethnicity an allele was first identified* | https://www.ebi.ac.uk/ipd/imgt/hla/ancestry/ | 10 |
| | | **Haplostats**<br>*Haplotype tool (based on USA population) to estimate likely haplotypes of patient, or find likely population for finding a matched donor* | http://www.haplostats.org | 19 |
| | | **Global distribution maps**<br>*Heatmaps of distribution of HLA alleles over the world* | http://pypop.org/popdata/ | 27 |

| | | | |
|---|---|---|---|
| **MATCHING** | **Statistics Search & Match Service**<br>*Statistics of database per organisation; useful to lookup the date of last update send to Search & Match, WMDA accreditation status.* | https://statistics.wmda.info | 30 |
| | **DPB1 T cell Epitope Algorithm**<br>*Calculator to predict permissive and non-permissive DPB1 mismatched between patient and donor. (other algorithm than in Search & Match Service)* | https://www.ebi.ac.uk/ipd/imgt/hla/matching/ | 10 |

Publisher: 2019 © WMDA 2019

**World Marrow Donor Association (WMDA)**
Schipholweg 57
2316 ZL Leiden
The Netherlands

T: +31 88 505 7900
E: education@wmda.info
W: www.wmda.info