

ALLAN: IMGT/HLA ALLele to UNOS ANtigen conversion tool (<http://www.transplanttoolbox.org/>)

Web Tool and Web Services User's Guide

Index

1. Overview
2. Resources
3. Web Tool
4. Antigen Probabilities
5. Web Services

Overview

The organ allocation computer matching system used by United Network Organ Sharing (UNOS) requires molecular HLA typing data of transplant candidates and donor organs to be reported as UNOS antigen equivalents for entry into UNetsm. This web tool maps ambiguous or unambiguous HLA typing data to respective antigens based on UNOS OPTN guidelines. A list of UNOS antigen equivalents is returned as output. Ambiguous typings use National Marrow Donor Program (NMDP) allele frequencies to calculate antigen probabilities and assign the most probable antigens for each locus.

Resources

An Organ Procurement and Transplantation Network (OPTN) policy documentation lists the guidelines that are the basis for the UNOS antigen assignments provided (1). The OPTN document in turn points to other resources including the IMGT/HLA database, which maintains World Health Organization (WHO) and World Marrow Donor Association (WMDA) antigen assignments for every allele (2). Some antigen assignments are also referenced in the 2008 HLA Dictionary (3). HLA allele frequencies for 26 US populations were obtained from NMDP (4)

Web Tool

Users can input HLA typing in a variety of formats: either a unambiguous single allele, a list of unambiguous alleles, genotype list string (GL string) (5) or NMDP multiple allele codes (MACs, <https://hml.nmdp.org/MacUI/>). The unambiguous alleles should be either full field IMGT/HLA nomenclature or high resolution (2nd field). Protein expression characters (L, N, Q, S) and characters specifying antigen recognition domain equivalents ("G", "P", "g") can be included before entry.

Allele: For antigen mapping for single alleles, click on "Allele" button on the home page or navigation bar, then enter the allele in the text box and click "Convert". The output shows the original IMGT/HLA allele and the UNOS antigen assignment. Bw4 or Bw6 epitopes are listed for HLA-B alleles.

List of Alleles: For mapping a list of HLA alleles, click on the "Alleles List" on home page or navigation bar, enter the list of alleles delimited by single space in the text box and click "Convert". The output shows the original IMGT/HLA alleles and the UNOS antigen assignments. Bw4 or Bw6 epitopes are listed for HLA-B alleles.

GL Strings: For mapping ambiguous HLA typing data represented in GL String format, click on the “Genotype List String”, enter the GL String for loci typed from A, B, C, DRB1, DRB3/4/5, DQB1 in the text box, select a US population using the dropdown menu, and click “Convert”. The GL string can be with or without prefix “HLA-”. The output will show the input GL string and population, the most probable UNOS antigen assignments, and full distribution of possible UNOS antigen assignments and their probabilities. Bw4 or Bw6 epitopes are listed for HLA-B alleles. The list of NMDP populations and acronyms are given in Table 1.

NMDP MACs: For mapping allele codes to antigens click on “Multiple Allele Codes” and enter a list of allele codes for loci typed from A, B, C, DRB1, DRB3/4/5, DQB1. Select the NMDP population and click on “Convert”. The allele codes should be delimited by single space, and allele codes from the same locus should be mentioned consecutively. The output is similar to GL string output and will show the input MACs and population, the most probable UNOS antigen assignments, and full distribution of possible UNOS antigen assignments and their probabilities. Bw4 or Bw6 epitopes are listed for HLA-B alleles. The list of NMDP populations and acronyms are given in Table 1.

UNOS Antigen Probabilities: UNOS antigen probabilities are calculated based on NMDP published HLA allele frequencies after conversion to UNOS antigen equivalents. Antigen probabilities for the same ambiguous HLA typing may differ based on the population selected because HLA allele frequencies differ by population.

Web services: User interface for “ALLAN” web services is available at http://www.transplanttoolbox.org/tool_services. The web services can be accessed through curl or HTTPie command line tools for example a “POST” request for antigen for “B*07:02” allele can be made with either of the following two commands:

- `http -f POST http://transplanttoolbox.org/single_allele/ allele=B*07:02`
- `curl -X POST http://transplanttoolbox.org/single_allele/ -d '{"allele": "B*07:02"}' -H 'Content-Type: application/json'.`

A demo python script is available at our git repository (https://github.com/lgragert/hla-who-to-unos/blob/master/conversion_services.py).

Table 1: NMDP Population Acronyms for 26 race/ethnic categories (5 broad and 21 detailed)

Acronym	NMDP Population
Broad Races	
AFA	African American
API	Asia/Pacific Islander
CAU	Caucasian
HIS	Hispanic
NAM	Native American
Detailed Races	
AAFA	African American
AFB	African
AINDI	South Asian Indian
AISC	American Indian-South or Central Am
ALANAM	Alaska Native
AMIND	North American Indian
CARB	Caribbean Black
CARHIS	Caribbean Hispanic
CARIBI	Caribbean Indian
EURCAU	European Caucasian
FILII	Filipino
HAWI	Hawaiian or Pacific Islander
JAPI	Japanese
KORI	Korean
MENAF	Middle Eastern or N. Coast of Africa
MSWHIS	Mexican or Chicano HIS
NCHI	Chinese
SCAHIS	Hispanic
SCAMB	South or Central American
SCSEAI	South east Asian
VIET	Vietnamese

References

1. Helman SW, Pollack MS. Interpretation of HLA typing Results for Entry into UNet-OPTN [Internet]. 2003 [cited 2017 Dec 12]. p. 1–10. Available from: <https://optn.transplant.hrsa.gov/resources/guidance/interpretation-of-hla-typing-results-for-entry-into-unet/>
2. Robinson J, Halliwell JA, Hayhurst JD, Flicek P, Parham P, Marsh SGE. The IPD and IMGT/HLA database: Allele variant databases. *Nucleic Acids Res.* 2015;43(D1):D423–31.
3. Holdsworth R, Hurley CK, Marsh SGE, Lau M, Noreen HJ, Kempenich JH, et al. The HLA dictionary 2008: A summary of HLA-A, -B, -C, -DRB1/3/4/5, and -DQB1 alleles and their association with serologically defined HLA-A, -B, -C, -DR, and -DQ antigens. *Tissue Antigens.* 2009;73(2):95–170.
4. Gragert L, Madbouly A, Freeman J, Maiers M. Six-locus high resolution HLA haplotype frequencies derived from mixed-resolution DNA typing for the entire US donor registry. *Hum Immunol.* 2013;74(10):1313–20.
5. Milius RP, Mack SJ, Hollenbach JA, Pollack J, Heuer ML, Gragert L, et al. Genotype List String : a grammar for describing HLA and KIR genotyping results in a text string. 2013;