



HAAMU: HLA allele to antigen mapping for UNOS

Users guide

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Overview

The organ allocation computer matching system used by United Network Organ Sharing (UNOS) requires the transplant recipients' and patients' data as acceptable and unacceptable human leucocyte antigens (HLA). This elicits the need to map DNA typed HLA alleles to their respective antigens. UNOS documentation enlists certain guidelines and few alleles to antigens conversions to be followed for entering antigens to UNetsm. Taking these guidelines into consideration, the HAAMU web tool maps the HLA typing data to respective antigens. Users can input either a single allele, list of alleles, genotype list string (gl string) or multiple allele codes (MACS) and get the respective antigens as output. Ambiguous typings in the form of gl strings and MACS are handled by taking National Marrow Donor Program (NMDP) alleles frequencies into consideration for calculating antigen probabilities and assigning the most common antigen.

Resources

Organ procurement and transplantation network (OPTN) policies documentation was used for antigen assignment guidelines. The link for the same is:

https://www.transplantpro.org/wp-content/uploads/sites/3/Policy_Notice_07-2015.pdf

Current updated list of HLA alleles was obtained from IMGT/HLA database (International Immunogenetics Information System), maintained by Anthony Nolan Research Institute. Allele frequencies for 25 US populations were obtained from National Marrow Donor Program.

How to use the HAMMU tool

Using HAMMU for antigen mapping is very convenient. Users can input the data as single allele, list of alleles, gl strings and MACS. The allele in the input should be either high resolution allele or medium resolved to specific HLA protein field. Protein expression specifying characters L, N, Q, S can be used but suffixes for P and G groups should be ripped off before entry.

Allele: For antigen mapping for single allele, click on “Allele” button on home page, then enter the allele and click “Convert!”. The output shows the allele the user wants to map, the antigen to which it is mapped as well as if Bw4 or Bw6 epitopes are present on the HLA antigen.

List of alleles: For mapping n number of alleles, click on the “Allele list” on home page, enter list of alleles delimited by single space and click “Convert!”. The output shows the list of alleles entered, the antigens to which alleles have been mapped by the tool and the presence of Bw4 or Bw6 epitopes is indicated.

GL Strings: For mapping HLA typing data as gl strings to antigens, click on the “Genotype List String” and enter the gl string in the text area. The gl string can be with or without prefix “HLA-”, however the string should indicate 3 or 4 or 5 or 6 loci typing in the prescribed formatx(Milius et al., 2013). Select the population typed for and click on “Convert!”. The output will show the gl string and population given as input, the antigens that were mapped to and presence of Bw4 or Bw6 epitopes. Keys to the acronyms of the populations is given in Table 1.

MAC: For mapping allele codes to antigens click on “Multiple Allele Codes” and enter the allele codes for 3 or 4 or 5 or 6 loci typed HLA data. Select the population and click on “Convert!”. The allele codes should be delimited by single space and allele codes from a single locus should be mentioned consecutively. The output is similar to gl strings and it shows the list of allele codes and population entered as input, the antigens mapped to the allele codes and presence of Bw4 or Bw6 epitopes.

Antigen probabilities: Antigen mapping for ambiguous HLA typing reported in gl strings and MACs was done by pulling the commonest antigen based on the population allele frequencies (Gragert, Madbouly, Freeman, & Maiers, 2013). Genotype combinations were derived from the gl strings or MACs followed by calculation of population specific genotype frequencies as well as antigen mapping for genotypes. Cumulative genotype frequencies were calculated for duplicate antigen-genotypes and antigens from the most common antigen-genotype were reported as mapped antigens for ambiguous HLA typing.

References

- Gragert, L., Madbouly, A., Freeman, J., & Maiers, M. (2013). Six-locus high resolution HLA haplotype frequencies derived from mixed-resolution DNA typing for the entire US donor registry. *Human Immunology*, 74(10), 1313–1320.
<https://doi.org/10.1016/j.humimm.2013.06.025>
- Milius, R. P., Mack, S. J., Hollenbach, J. A., Pollack, J., Heuer, M. L., Gragert, L., & Spellman, S. (2013). Genotype List String : a grammar for describing HLA and KIR genotyping results in a text string. *Tissue Antigens*, 82(2), 106-112.
<https://doi.org/10.1111/tan.12150>

Table 1: Key for population acronyms

Acronym	Population
AAFA	African American
AFA	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
CAU	Caucasian
EURCAU	European Caucasian
FILII	Filipino
HAWI	Hawaiian or Pacific Islander
HIS	Hispanic
JAPI	Japanese
KORI	Korean
MENAF	Middle Eastern or N. Coast of Africa
MSWHIS	Mexican or Chicano HIS
NAM	Native American
NCHI	Chinese
SCAHIS	Hispanic
SCAMB	South or Central American
SCSEAI	South east Asian
VIET	Vietnamese