VICTOR: VIrtual CrossmaTch for mOleculaR typing data

(http://www.transplanttoolbox.org/victor)

Web Tool and Web Services User's Guide

Index

Overview

Virtual crossmatch (VXM) is a prediction of physical crossmatch by cross referencing donor's HLA typing with candidate's unacceptable antigens (UAs). This algorithm is rather complex as the donor typing is often ambiguous with long strings of possible alleles, which should be mapped to their serological equivalents. The UAs should also be mapped to Organ Procurement and Transplantation Network (OPTN) defined equivalents (OPTN policy 4, Tables 4-5 to 4-11)(1). The UAs may comprise of allele level specificity. After all the mappings, the propensity of VXM for each conflict between donor typing and UAs is allele frequency dependent, which varies ethnically. We have made a user friendly tool to compute VXM for unambiguous and ambiguous HLA typing. This tool gives probability of positivity of VXM for each conflicting antigen (CA).

Resources

Mapping tables for IPD-IMGT/HLA alleles to UNOS antigens and reverse mapping table for UNOS antigens to IPD-IMGT/HLA alleles were obtained from ALLAN (http://www.transplanttoolbox.org/allan) (2). OPTN UA equivalents were obtained from policy document(1). HLA allele frequencies for 26 US populations were obtained from NMDP(3).

Web Tool

Users can input donor HLA typing for unambiguous and ambiguous cases. The unambiguous typing can either be UNOS serological equivalents or high resolution HLA alleles (two-field resolved or full IPD-IMGT/HLA allele). The ambiguous HLA typing includes genotype list string (GL string)(4) and NMDP mulitiple allele codes (NMDP-MACS)(5). Protein expression characters (L, N, Q, S) and characters specifying antigen recognition domain equivalents ("G", "P", "g") can be included for entry of high resolution alleles and GL string as applicable. The UAs of the candidate can be serologic determinant or alleles as detected by single antigen beads. For ambiguous HLA typing, donor ethnicity should also be selected from one of the 5 broad races or one of the 21 detailed races depending on the information available. The keys for race acronyms are mentioned in Table 1.

Unambiguous donor HLA typing

UNOS Antigen Equivalents and High Resolution Alleles: If donor typing is available as UNOS antigen equivalents or high resolution alleles, enter donor typing in the first text box and candidate's UAs in the second text box then click "Submit". The output shows donor's typing that was entered, candidate's UA including the OPTN equivalents and VXM negativity or positivity if there are CAs.

Ambiguous donor HLA typing

GL Strings and NMDP MACS. To compute VXM when donor typing is available as GL string or MACS, enter the donor typing in first text box, candidate's UA in the second text box. Select donor's race/ethnicity, enter a probability threshold and click "Submit". The output shows donor's parameters i.e. typing entered and ethnicity selected, candidate's UAs and OPTN equivalents mapped, VXM positivity or negativity alongwith CAs. The table shows probability of VXM positivity for each CA that is above the user defined threshold.

VXM Probabilities: VXM probabilities are calculated based on NMDP published HLA allele frequencies after conversion to UNOS antigen equivalents. VXM 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 **"**VICTOR" web services is available at http://www.transplanttoolbox.org/victor/services. The web services can be accessed through curl or HTTPie command line tools. An example "POST" request for donor typing as GL string can be made with either of the following commands:

- http -f POST http://transplanttoolbox.org/string_gl_victor/ Donor_GL_string="A*02:01g+A*26:01g|A*02:55+A*26:07^C*05:01g+C*01:02g^ B*15:01/B*15:02/B*15:03/B*15:04+B*27:05g^ DRB1*12:01g+DRB1*01:01^DQB1*03:01g+DQB1*05:01" Donor_ethinicity=CAU Candidate_Unacceptable_antigens="A210 Bw4 B40 DR3 DQ5"

- curl -X POST http://transplanttoolbox.org/string_gl_victor/ -d '{"Donor_GL_string": "A*02:01g+A*26:01g|A*02:55+A*26:07^ C*05:01g+C*01:02g^B*15:01/B*15:02/B*15:03/B*15:04+B*27:05g^DRB1*12:01g+DRB1*01:01^DQB1*03:01g+DQB1*05:01", "Donor_ethinicity": "CAU", "Candidate_Unacceptable_antigens": "A210 Bw4 B40 DR3 DQ5"}' -H 'Content-Type: application/json'

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 Black
AINDI	South Asian Indian
AISC	American Indian-South or Central American
ALANAM	Alaska Native or Aleut
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
MENAFC	Middle Eastern or N. Coast of Africa
MSWHIS	Mexican or Chicano
NCHI	Chinese
SCAHIS	Hispanic- South or Central American
SCAMB	South or Central American
SCSEAI	Southeast Asian
VIET	Vietnamese

References

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3. 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.
4. 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;
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