

A PC BASED PROGRAM TO MATCH HIGHLY SENSITIZED KIDNEY PATIENTS WITH POTENTIALLY COMPATIBLE DONORS

J. Kreuziger, K. Holden and E. Klohe, Inland Northwest Blood Center, Spokane, WA.

Introduction

Highly sensitized kidney patients ($\geq 80\%$ PRA) represent a tremendous challenge with respect to identifying compatible donors. Extra points for high PRA and waiting time improve the odds of allocation once a compatible donor is identified. However, only access to a larger donor pool will increase the likelihood of identifying compatible donors.

Attempts at regional sharing for high PRA patients have been hampered by the significant rate of positive final crossmatches. The UNOS Histocompatibility Committee is testing the theory that *permissible donor mismatches* can be used as a basis for matching to accurately predict final crossmatch results. If final crossmatch results can be accurately predicted, the UNOS kidney allocation system could be modified to identify and allocate compatible *non-local* donors to highly sensitized patients.

Permissible donor mismatches are identified by excluding known unacceptable antigens and including known acceptable antigens from a list of all potential mismatched donor antigens. This process leaves a group of antigens of *unknown acceptability* that can be evaluated by crossmatches with partially mismatched cells. We developed a software program that helps identify those cells that would be useful to determine antigen acceptability for the highly sensitized patients on our waiting list.

Materials and Methods

As a participant in the feasibility study, potential *permissible donor mismatches* were identified for each of the highly sensitized patients on our waiting list. These included antigens closely related to the patient's own antigens such as alternate splits and members of limited cross-reactive groups (CREGS) and/or antigens proven to be permissible based on negative flow cytometric bead or cell antibody identification panels. Unacceptable antigens were identified by use of

antibody screening methods with sensitivity equal to those of final crossmatches and careful specificity analysis that included consideration of antibodies directed against public epitopes and antigens within CREGS.

Our software program allows us to enter the HLA-A, B and DR antigens of every cell typed within our laboratory (e.g. organ, platelet or stem cell donor, patients, employees) and search the highly sensitized patient database for potential compatibility based on matching only the patient's own antigens and either *permissible donor mismatched* or *acceptability unknown* antigens. Once a match is found, a flow cytometry crossmatch is performed to confirm *permissible donor mismatches* or re-classify *acceptability unknown* mismatched antigens as either permissible or unacceptable.

The program is a custom Microsoft Access™ database application and is run on a Windows 2000 facility network. Logic to match both the patient's own antigens and identified *permissible donor mismatches* or *acceptability unknown* antigens with the cell donor's antigens was incorporated. The program allows the list of *permissible donor mismatches* and *acceptability unknown* antigens for each patient to be edited if new antibody specificities are either identified or ruled out based on crossmatch results.

Results

Table 1 is an example of a highly sensitized patient's initial data, including HLA type, PRA, and preliminary antibody identification. Based on this data, a preliminary set of unacceptable antigens is defined. Preliminary *permissible donor mismatches* are identified based on limited CREG matching and non-self antigens present on non-reactive flow-specific beads (table 2). Next a list of *acceptability unknown* mismatches is created which consists of antigens that are neither unacceptable nor *permissible donor mismatches* (table 3). The software identifies cell donors to crossmatch with the patient to confirm *permissible donor mismatches* or evaluate *acceptability unknown* antigens. Table 4 shows the HLA types of cells identified by the software, the flow crossmatch result, and the action taken. For this patient, B51 was moved to the unacceptable antigen list and A29 was moved to the *permissible donor mismatches* list.

Conclusion

After evaluating as many *antigens of acceptability unknown* as possible, those remaining are considered unacceptable. Then the patient is ready to be entered into a regional sharing system for consideration of kidneys from donors with only

self- or confirmed *permissible donor mismatched* antigens. The program may be adaptable for use by other laboratories or within sharing regions in advance of a UNOS-wide system.

Patient Data	
HLA Type	A1,2 B37(w4),44(w4) DR4,15
Sensitization	0 transplants, 0 transfusions, 1 pregnancy
Husband's HLA Type	A2,24 B7(w6) DR4,15
Commercial frozen T-cell tray / AHG Antibody ID	PRA = 40% B7, 42, 60, 61
Local T-cell panel / AHG Antibody ID	PRA = 80% Bw6
Flow PRA I/II Flow PRA Specific Antibody ID	PRA = 67% / 0% B27, Bw6
Unacceptable Antigens	A24 B7, 27, 42, 60, 61, Bw6
Table 1. Patient's HLA typing information and antibody screen results.	

Preliminary <i>Permissible Donor Mismatches</i>	
<i>Permissible Donor Mismatches</i>	Rationale
A1,2 B37,44 DR4,15	Self HLA antigens
All DR antigens	0% Flow PRA II
A11, 36, 28, 68, 69	HLA-A locus limited CREG matches
B47, 49	HLA-B locus limited CREG matches
A11,23 B49,52 ; A34,74 B57 ;	Non-self antigens present on non-reactive flow

A32,68 B47

PRA specific beads.

Table 2. Preliminary listing of *permissible donor mismatches* based on limited CREG matching and antibody screen results.

Acceptability Unknown Mismatches

HLA Locus	Mismatch
HLA-A	A3, 25, 26, 29, 30, 31, 33, 66, 80
HLA-B	B13, 38, 51, 53, 58, 63, 77

Table 3. Listing of *acceptability unknown* mismatches that have not been ruled as unacceptable antigens or *permissible donor mismatches*.

Donors Identified For Flow Crossmatch

Donor HLA Type	Flow Crossmatch Result	Action Taken
A2 B44,51	POSITIVE	Move B51 to unacceptable antigen list
A1,29 B44	NEGATIVE	Move A29 to <i>permissible donor mismatch</i> list

Table 4. Donors with *acceptability unknown* mismatches identified for flow crossmatches and the action taken based on the crossmatch result.