

HLA-A, B, C, DR AND DQ "SPLIT" SPECIFICITY LEVEL MATCHING IN HLA-A,B,DR "FAVOURABLY MATCHED" KIDNEY RECIPIENTS



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Introduction

"Favourable" kidney recipient/donor HLA matching in the UK allocates kidneys with A,B,DR mismatch grades of 000, 010, 110, largely at the "broad" specificity level. Although it is accepted that additional mismatching will occur at the level of "split" specificities it is often assumed that, due to strong linkage disequilibrium, matching for HLA-B and DR will result in good matching for HLA-C and DQ, respectively.

To assess the actual level of split specificity mismatching for HLA-A,B,C,DR and DQ in "well matched" donor/recipient pairs we studied a group of favourably matched recipients and their donors.

Methods

The level of mismatching for HLA-A,B,C,DR,DQ "splits" was investigated in 201 favourably matched first graft cadaveric donor/recipient pairs transplanted between 1985 and 1999 (000 n=39, 100 n=42, 010 n=49, 110 n= 71).

Split specificity level typing was performed for HLA-C (Cw1-Cw18), DR and DQ by DNA-based methods and A,B typing was done by PCR-SSP and/or serology.

Using local HLA-B/C and DR/DQ linkage disequilibrium data the likely HLA-B/C and DR/DQ haplotypes(s) responsible for the HLA-C and DQ mismatch(es) were established for each transplant pair.

Results

Of the 000 mismatched pairs none had additional A,B,DR split mismatches, but 35.9% (n=14) and 20.5% (n=8) had at least one HLA-C or DQ mismatch, respectively.

All the DQ mismatches in the 000 group were due to the presence of DR4 in association with DQ7 and DQ8. HLA-C mismatches were due to HLA-B/C haplotypes possessing HLA-B44 (n=9), HLA-B7 (n=3), HLA-B5 (n=2), HLA-B27 (n=1) and HLA-B17 (n=1) -1 case of two mismatches.

In the 100 and 010 groups there were 17 additional instances of B or A mismatches and 5 additional DR split mismatches.

One broad A or B mismatch in the 100 and 010 groups made a significant difference (p<0.01) to the presence of B and A split mismatches, respectively, but no significant difference (p>0.4) to the presence of a DR split mismatch.

Overall, 67.2% of the total group had at least one HLA-C mismatch. This included: 39.5% (000 n=14, 100 n=18) of the 81 cases broadly matched for HLA-B and 85.8% (010 n=42, 110 n=61) of the 120 patients mismatched for HLA-B (p<0.0001).

27.4% (000 n=8, 100 n=8, 010 n=18, 110 n=21) of the total group of 201 had at least one DQ mismatch. The HLA-DR/DQ haplotypes resulting in an DQ mismatch were HLA-DR4, seen in association with HLA-DQ7 and DQ8 (n=39), HLA-DR7 in association with DQ2 and DQ9 (n=12), DR6 (n=9) in association with DQ5, DQ6, and DR2 (n=2) in association with DQ5 and DQ6 (Table 1).

Table 1. Percentage of favourably matched donor/recipient pairs with at least one HLA-A,B,C,DR, or DQ split mismatch.

UKTSSA mismatch grade (A,B,DR)	HLA-					No.
	A	B	DR	C	DQ	
000	0	0	0	35.9	20.5	39
100	100.0	14.3	4.8	42.9	19.0	42
010	16.3	100.0	6.1	85.7	36.7	49
110	100.0	100.0	5.6	85.9	29.6	71

Comments

Although, as expected, the presence of an HLA-B mismatch had a profound effect on the level of HLA-C mismatching almost 40% of HLA-B matched patients were mismatched for HLA-C.

In addition, 27.4% of the total group had at least one DQ split mismatch. The level of split DQ matching was not significantly influenced by the presence of an A, B broad or split or a DR split mismatch. However, the frequency of broad DQ mismatches were significantly increased (p<0.05) in the presence of a broad B mismatch.

Thus, considerable HLA-A,B,C,DR,DQ matching heterogeneity exists, even amongst the most favourably matched patient groups.

These findings highlight the importance of accurately differentiating patients' antibodies.

Further, little is known of the effects on graft survival of combinations of mismatched specificities particularly those involving HLA-C and DQ.