

Relationship between the complement dependent cytotoxicity (CDC), Luminex single antigen bead (SAB) and Luminex C1q assays



B Rana, C Darke, MT Rees, F Edwards, E Burrows



WELSH TRANSPLANTATION AND IMMUNOGENETICS LABORATORY



Introduction

The CDC assay detects complement fixing HLA antibodies and CDC-defined DSAs are considered a contraindication to renal transplantation. In contrast, the highly sensitive SAB detects both complement fixing and non-complement fixing antibodies but their clinical significance is controversial. The C1q assay detects antibodies that bind C1q. We examined the relationship between these three tests.

Methods

111 samples from renal patients were tested by CDC using B-cells (with/without DTT), also Class I and II SAB (with serum EDTA pre-treatment) and the C1q assay (One Lambda).

Results

Table 1: Total number of IgG specificities detected by the CDC, C1q and SAB assays

Antibody specificities	CDC	Luminex SAB	C1q
HLA-A	14	265	81
HLA-B	10	415	87
HLA-C	1	88	5
HLA-DR	6	207	25
HLA-DRB3/4/5	0	43	7
HLA-DQ	7	412	183
HLA-DP	0	241	59
Total no. of specificities	38	1671	447

Overall, 38 IgG specificities were detected by CDC (covering HLA-A,B,C,DR,DQ), 1,671 by SAB and 447 (26.8% of SAB specificities) by the C1q assay (both covering HLA-A,B,C,DR,DR51/2/3,DQ,DP) – Table 1

The Luminex SAB detected all the CDC defined specificities. However, the C1q assay failed to detect 26% (10/38) of the CDC-defined IgG antibodies. Also, only two of the seven IgM specificities identified by CDC were C1q assay positive.

Table 2: Total number of specificities above or below 10,000 MFI by the Luminex SAB assay and their ability to bind C1q

Luminex SAB MFI	C1q positive specificities		C1q negative specificities	
	Class I	Class II	Class I	Class II
>10,000	159	255	42	47
<10,000	14	19	553	582
PPV=93%			NPV=93%	

82% (414/503) of the SAB specificities with a MFI>10,000 were C1q binding whereas, only 3% (33/1,168) of SAB specificities with an MFI<10,000 were C1q binding – Table 2.

Conclusion

An important association was found between high Luminex SAB MFIs and the ability to bind C1q. Overall, a SAB MFI of >10,000 for a given HLA specificity had a positive predictive value of 93% for that specificity being positive in the C1q assay.