American Journal of Transplantation 2006; 6: 2947–2954
Blackwell Munksgaard

© 2006 The Authors
Journal compilation © 2006 The American Society of
Transplantation and the American Society of Transplant Surgeons

doi: 10.1111/j.1600-6143.2006.01560.x

Development of Nondonor-Specific HLA-DR Antibodies in Allograft Recipients Is Associated with Shared Epitopes with Mismatched Donor DR Antigens

J. Cai[a], P. I. Terasaki[a,*], Q. Mao[a], T. Pham[a], N. El-Awar[b], J.-H. Lee[b] and L. Rebellato[c]

[a] *Terasaki Foundation Laboratory, 11570 W Olympic Blvd. Los Angeles, California, USA*
[b] *One Lambda Inc, Canoga Park, Los Angeles, California, USA*
[c] *Department of Pathology, The Brody School of Medicine at East Carolina University, Greenville, North Carolina, USA*
* *Corresponding author: Paul I. Terasaki, terasaki@terasakilab.org*

Our previous studies showed that not only donor-specific antibodies (DSA) but also nondonor-specific antibodies (NDSA) were detected in the peripheral blood of allograft recipients. The molecular mechanism involved in the development of NDSA is examined here. HLA class II single antigen (SA) beads were used to determine the presence of HLA DR-specific antibodies in renal transplant recipients with failed allografts. Sequence-based antibody-epitope mapping was determined by the comparison of the reaction profiles of different SA recombinant cell lines containing unique epitope pattern. We found that 22 out of 65 recipients with failed grafts developed antibodies against donor HLA DR that is a mismatch with the recipient. Three of them had only DSA while 19 patients had not only DSA but also NDSA. An average of 77.3% of NDSA reacted with targets that share amino acid sequence with mismatched donor DR antigens. Either surface or nonsurface amino acid residues may constitute an antibody epitope. In conclusion, development of NDSA in allograft recipients may be associated with shared amino acids with mismatched donor antigens. SA beads technique not only helps to determine antibody specificities but also provides an ideal approach for the identification of potential HLA antibody epitopes.

Key words: **Antibody epitope, donor-specific antibody, graft failure, nondonor-specific antibody, rejection**

Abbreviations: **HLA, human leukocyte antigen; DSA, donor-specific antibody; NDSA, nondonor-specific antibody; MM, mismatched; SA, single antigen.**

Received 16 June 2006, revised 17 July 2006 and accepted for publication 3 August 2006

Introduction

Previous studies have suggested a positive correlation between the development of alloantibodies and transplant rejection (1–4). The numeric relationship between serum creatinine and donor-specific antibody (DSA) levels further suggests a causal relationship between the presence of alloantibody and renal transplant rejection (5). Therefore, alloantibody monitoring in allograft recipients posttransplantation becomes extremely important. It will help clinicians to determine a patient's humoral responses against allograft and, more importantly, it may direct clinicians to optimize and/or minimize immunosuppressive drug therapy (6,7).

When monitoring alloantibodies in transplant recipients, a common phenomenon has been found that not only DSA but also nondonor-specific antibody (NDSA) were detected in the peripheral blood (5,8,9). The goals of this study were to determine the epitope specificity of HLA-DR DSA in the sera of recipients with failed renal allograft and also to determine the correlation between the development of DSA and NDSA.

To achieve these goals we used the recently developed color-coded microspheres coated with single HLA antigens to identify the HLA-DR antibodies present in the sera of recipients with failed allografts. Potential epitopes of DSA were mapped by comparing the amino acid sequences of the recipient and donor DR allele(s). A potential epitope is an amino acid(s) that is (are) present in a given location of the donor DR but are not present in the recipient. To verify the potential epitopes we used a combination of different single antigen (SA) recombinant cell lines that have a unique epitope pattern.

Materials and Methods

Allosera and SA beads assay

A total of 65 sera obtained from renal transplant recipients with failed grafts were tested for antibody specificities using the HLA class II SA beads (LABScreen® beads, One Lambda Inc., Canoga Park, CA). LABScreen assay was performed according to the manufacturer's protocol. In brief, 20 μL of 1:3 diluted sera was added to 2.5 μL of antigen beads, incubated in the dark for 30 min at room temperature (RT), and then washed with wash buffer. One hundred microliters of PE-conjugated goat anti-human IgG 2nd antibody

were added to the beads, incubated for 30 min in the dark at RT, washed and read on the LABScreen™ 100 Luminex (One Lambda Inc.).

Antibody elution

Allosera (20 μL, 1:3 dilution) were incubated with recombinant SA expressing cell lines at RT for 30 min. The cells were washed with PBS and the absorbed antibodies were eluted by mixing 60 μL of ImmunoPure IgG Elution Buffer (Pierce, Rockford, IL) with cells and incubated for 10 min at RT. After incubation, the eluted antibody was separated from cells by centrifugation, removed and neutralized with 3 μL of 1 M Tris-HCl (pH 9.5). Twenty microliters of the eluted antibody was then tested for antibody specificities using SA beads following the manufacturer's protocol as described above.

Potential epitope identification

HLA-DR amino acid sequences were obtained from the HLA Informatics group section at the Anthony Nolan website (http://www.ebi.ac.uk/imgt/hla/funding.html). By comparing the amino acid sequences of a group of HLA-DR alleles that are either recognized or not by the alloserum, a likely epitope was deduced. Potential antibody epitopes were verified by antibody reaction profiles with a combination of SA recombinant cell lines that contain a unique epitope pattern.

Cytotoxicity testing

The Terasaki tray was coated with 1 μL of patient's sera. To each well, 1 μL of a 2×10^6 cells/mL suspension of SA cells was added. The microdroplets were mixed together using an electrostatic mixer of a wire. The tray was incubated at RT for 1 h. Corresponding rabbit complement was added to each well of the test tray and tray was incubated at RT for 2 h. After incubation, 5 μL of FluoroQuench AO/EB (One Lambda Inc.) was added for fluorescence testing. The reading was assigned based on the percent killing of target cells according to the following formulae: '−': 0–10%; '−/+': 10–20%; '+':20–50%; and '++': 50–100%.

Results

A total of 65 sera from recipients with failed grafts were tested for the presence of HLA-DR antibodies. Twenty-two out of 65 recipients' sera had detectable antimismatched donor DR specific antibodies (Table 1). Three sera had only DSA (ID14, 15 and 21) while the others had both DSA and NDSA. Sequence-based antibody-epitope mapping indicated that 77.3% of NDSA reacted with targets that share amino acid sequence with mismatched donor DR antigens (underlined).

Table 2 shows the list of all potential donors' DR specific antibody epitopes which were identified by sequence-based epitope mapping. Among the 79 identified potential DR antibody epitopes, a single amino acid determinant accounted for 74.7% (59/79), while 2, 3 and 4 amino acid determinants accounted for 17.7%(14/79), 6.3%(5/79) and 1.3%(1/79), respectively. To investigate the importance of the amino acid location in determining an antibody epitope, the presence of amino acid location in constituting either one or multiple amino acid antigenic determinants were counted and the top 30 most frequent amino acid locations are listed in Table 3. Interestingly, 13 of 30 residues are on

Table 1: DSA and NDSA in kidney transplant recipients with failed grafts

			Anti-DR antibodies	
ID	Pre-Tx PRA%	mmDR	DSA	NDSA
1	0	15	15	1,4,7,8,9,10,11,12,13,14,16,103,51,53
2	0	13	13	11,14,17
3	0	10,17	10,17	4,7,8,9,11,12,13,14,18,52,53,16
4	13	1,8	1,8	4,11,12,13,14,17,18
5	0	1	1	9,10,51,53,4,14,15
6[1]	12	7,13	7,13	8,9,11,12,14,15,17,18,10,51
7	0	13	13	4,8,11,12,14,15,16,17,18,52,51
8[1]	0	1,4,5	4	7,10,51,52,8,9,14,17
9	0	10	10	4,7,9,14,51,53,1,15
10	0	1	1	103,4,10,53
11	0	15	15	1,7,9,51,52,53,103,8,13
12	0	13,15	13,15	51
13	0	2	2	1,4,7,9,10,51,53,103
14	0	4	4	N/A
15	0	6	6	N/A
16	0	11,16	16	52
17	11	8	8	12
18	0	4,7	4,7	9,10,12,14,53,1,8,51
19	0	1	1	9,10,51,53,4,8,14,16
20	0	7	7	9,53,4
21	0	13,14	13	N/A
22	95	7,14	7	1,9,10,15,16,51.52,53,4,8

[1] Retransplant.

Pre-Tx PRA% =pre-transplant panel reactive antibodies (class I/II)%; mmDR = mismatched DR; DSA = donor-specific antibody; NDSA = nondonor-specific antibody; underlined = NDSA sharing epitope(s) with DSA = 77.3% of all NDSA.

Table 2: Potential DSA epitopes and their relationship with NDSA

				NDSA (sharing or not sharing epitope(s) with drDR)	
ID	DSA	Cytotoxicity	DSA epitope(s)	Yes	No
1	DR15	+	**77T**	DR1,4,7,8,9,10,11,12,13,14,16,51,53	N/A
2	DR13	+	11S12T13S	DR11,14,17	N/A
3	DR17	++	9E10Y11S12T13S	DR11, 13, 14	DR16
			73G	DR7,17,52	
			77N	DR18,52	
			96H	DR7,8,9,11,12,13,14,18,52	
			140T	DR4,8,11,12,13,14,18	
			149H	DR8,11,12,13,14,18	
	DR10	+	**181M**	DR7,9,53	
4	DR1	+	85A	DR12	N/A
	DR8	+	10Y11S12T	DR11,12,13,14,17,18	
			149H	DR11,12,13,14,17,18	
			13G16Y	DR12	
			57S	DR4,13	
			74L	N/A	
			85A	DR12	
5	DR1	++	13F	DR9,10	DR4,14,15
			30C	N/A	
			31I	DR9,51,53	
			96E	DR51	
6	DR7	+	11G14K	N/A	DR10,51
	DR13	++	**25Q**	N/A	
			57V **60S**	DR9,12	
			78V	DR9	
			10Y11S12T	DR8,11,12,14,17,18	
			47F	DR11,12,15,17	
			149H	DR8,11,12,14,17,18	
7	DR13	–	12Y13S14T	DR 8, 11, 12, 14, 17, 18	DR51
			15S	DR 11, 14, 17, 18, 52	
			30D	DR 4, 8, 11, 14, 15, 16, 17	
			49F	DR 11, 12, 15, 17	
			59S	DR 4, 8	
			73K	DR 4, 17, 18, 52	
			151H	DR 8, 11, 12, 14, 17, 18	
8	DR4	+	11V	DR10	DR8,9,14,17
			98E	DR7	
			120N	DR10,51,52	
9	DR10	+	38A40Y	DR53	DR1,15
			70R	DR9,14	
			120N	DR4,51,53	
			173M	DR53	
			181M	DR7,9,53	
11	DR1	+	30C	DR103	DR4,10 (11V)
			96E	DR103	DR4,10,53 (120N)
11	DR15	+	9W	DR1,7,103	DR8,13
			140A	DR1,7,9,51,52,53,103	
12	DR13	++	N/A	N/A	N/A
13	DR2	++	71A	N/A	DR51
			9W10Q	DR1,7	N/A
			10Q	DR1,4,7,9,51,53,103	N/A
			11P13R	N/A	N/A
			37S	DR1,103	N/A
			96Q	DR10,53	N/A
			133I142M	N/A	N/A
14	DR4	+	11V13H	N/A	N/A
			96Y		
			180L		
15	DR6	–	67I70D71E	N/A	N/A
16	DR16	+	67F70D	N/A	DR52
			96Q	N/A	
17	DR8	+/–	13G16Y	DR12	N/A
18	DR7	+/–	**4Q**	DR9,53	DR1,8,51
			37F	DR14	
			57V **60S**	DR9,12	
			78V	DR9	
			181M	DR9,10,53	
	DR4	+/–	98E **104A**	DR9	

Table 2: Continued.

ID	DSA	Cytotoxicity	DSA epitope(s)	NDSA (sharing or not sharing epitope(s) with drDR)	
				Yes	No
19	DR1	+/−	13F	DR9,10	DR4,10,51,53 (120N) DR8,14,16
			31I	DR9,51,53	
			96E	DR51	
20	DR7	−	**4Q**	DR9,53	DR4
			78V	DR9	N/A
21	DR13	−	57S71K	N/A	N/A
22	DR7	+	**4Q**	DR9,53	DR4,8(57S)
			13Y	DR51	
			57V60 S	DR9	
			74Q	DR52	
			78V	DR9	
			140A	DR1,9,15,16,51,52,53	
			181M	DR9,10,53	

dr = donor; mm = mismatched; DR = HLA-DR; DSA = donor-specific antibody; NDSA = nondonor-specific antibody; bold text = surface residue.

Table 3: Top 30 amino acid locations constituting antigenic determinants for alloantibodies

Order	AA location	Frequency
1	13	9
2	11	7
3	**96**	6
4	57	5
5	**181**	4
6	78	4
7	12	4
8	10	4
9	149	3
10	**140**	3
11	**98**	3
12	71	3
13	**60**	3
14	30	3
15	9	3
16	4	3
17	120	2
18	85	2
19	**77**	2
20	74	2
21	**73**	2
22	**70**	2
23	**35**	2
24	31	2
25	16	2
26	14	2
27	**180**	1
28	**173**	1
29	**151**	1
30	142	1

Bold text = surface residue.

the antigen surface, while the other 17 were nonsurface residues.

Figures 1 and 2 show two examples of identified DR antibody epitopes. The first example is of a single amino acid determinant 77T, while the other is of a three amino acid determinant 11S,12T,13S. As shown in Figure 1, recipients and donors were mismatched for DR15. Studies using the Luminex class II SA beads indicated that the patient's serum had positive reactions against 20 SA beads (3–22). Alignment and comparison of the antigen sequences revealed that the antigens that the patient serum positively reacted with shared the same amino acid 'T' (Threonine) at position 77. This amino acid 77T is located at the top of the DR molecule. To further verify 77T as an antibody epitope, we used three recombinant cell lines, DRB1∗150201 (donor DR), DRB1∗010101 (nondonor DR), and DRB1∗070102 (nondonor DR), for absorption and elution testing. To accomplish this antibodies absorbed by the SA cell lines were eluted and tested again with SA beads. Interestingly, the eluted antibodies from these cell lines demonstrated exactly the same reaction pattern as the original serum. Each of these cell lines has a unique pattern of potential antibody epitopes. When comparing the amino acid sequence shared between them as well as the other positive antigens, but not the negative ones, it indicates that the target is the amino acid 77T. Therefore, these SA data from the original serum and the eluates from SA cell lines suggest that the mismatched donor DR15 antigen may cause the patient's antibody reaction against donor specific antigenic determinant-77T residue. The anti-77T DSA reacted with all DR antigens that have a T at position 77. In this case, T at position 77 was found in 20/23 DR antigens tested.

Figure 2 shows an identified potential antibody epitope associated with three amino acids (11S, 12T, 13S). SA bead tests with patient's sera and the antibodies eluted from recombinant cell lines showed the same reaction pattern. However, the antigen which shares only one (21, 13S) or two (3 and 15, 11S, 12T) amino acids with the identified potential epitope showed negative results, indicating that the epitope is associated with three amino acids. Noticeably, this three amino acid antigenic determinant is not found on the surface of the DR molecule, rather it is found on the bottom of the peptide-binding groove.

SA bead ID	SA beads	epitope	SA results	Absorption and elution from SA line/bead		
		77		DRB1*150201	DRB1*010101	DRB1*070102
1	^DRB1*030101	N	-	-	-	-
2	^DRB1*030201	N	-	-	-	-
3	#DRB1*150101	T	+	+	+	+
4	#DRB1*150201	T	+	+	+	+
5	DRB1*010101	T	+	+	+	+
6	DRB1*010201	T	+	+	+	+
7	DRB1*0103	T	+	+	+	+
8	DRB1*040101	T	+	+	+	+
9	DRB1*040501	T	+	+	+	+
10	DRB1*070101	T	+	+	+	+
11	DRB1*080101	T	+	+	+	+
12	DRB1*090102	T	+	+	+	+
13	DRB1*100101	T	+	+	+	+
14	DRB1*110101	T	+	+	+	+
15	DRB1*120101	T	+	+	+	+
16	DRB1*130101	T	+	+	+	+
17	DRB1*130301	T	+	+	+	+
18	DRB1*140101	T	+	+	+	+
19	DRB1*160101	T	+	+	+	+
20	DRB4*01030101	T	+	+	+	+
21	DRB5*010101	T	+	+	+	+
22	DRB1*0404	T	+	+	+	+
23	DRB3*0201	N	-	-	-	-

^:patient DR; #:mismathced donor DR

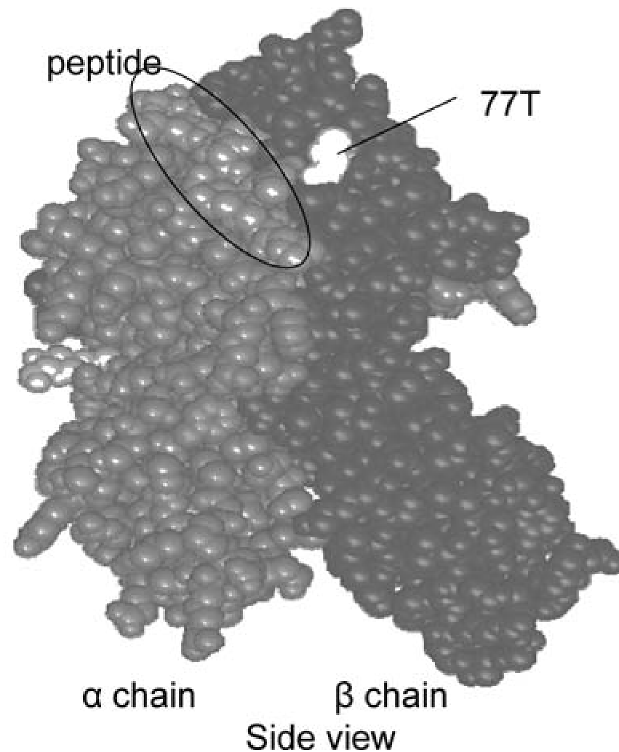

Figure 1: Identified DR epitope on the surface of molecule (ptDR:17,-; drDR:15,17).

SA bead ID	SA beads	epitope			SA results	Absorption and elution from SA line/bead	
		11	12	13		DRB1*130101	DRB1*140101
1	^DRB1*010101	L	K	F	-	-	-
2	^DRB1*010201	L	K	F	-	-	-
3	^DRB1*120101	S	T	G	-	-	-
4	#DRB1*130101	S	T	S	+	+	+
5	#DRB1*130301	S	T	S	+	+	+
6	DRB1*030101	S	T	S	+	+	+
7	DRB1*030201	S	T	S	+	+	+
8	DRB1*110101	S	T	S	+	+	+
9	DRB1*140101	S	T	S	+	+	+
10	DRB1*0103	L	K	F	-	-	-
11	DRB1*040101	V	K	H	-	-	-
12	DRB1*0404	V	K	H	-	-	-
13	DRB1*040501	V	K	H	-	-	-
14	DRB1*070101	G	K	Y	-	-	-
15	DRB1*080101	S	T	G	-	-	-
16	DRB1*090102	D	K	F	-	-	-
17	DRB1*100101	V	K	F	-	-	-
18	DRB1*150101	P	K	R	-	-	-
19	DRB1*150201	P	K	R	-	-	-
20	DRB1*160101	P	K	R	-	-	-
21	DRB3*0201	L	K	S	-	-	-
22	DRB4*01030101	A	K	C	-	-	-
23	DRB5*010101	D	K	Y	-	-	-

^:patient DR; #:mismathced donor DR

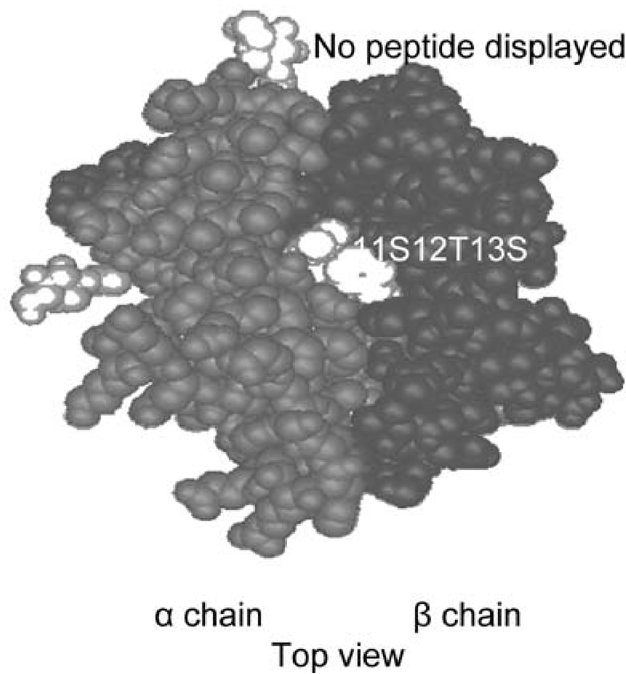

Figure 2: Identified DR epitope not on the surface of molecule (ptDR:1,12; drDR:13,-).

Discussion

Our previous study demonstrated that in patients with biopsy-diagnosed humoral rejection (C4d+), serum levels of both DSA and NDSA correlated with patient serum creatinine levels. Rejection treatment can reduce both DSAs and NDSAs and reverse humoral rejection. This numeric relationship between serum creatinine and HLA antibody levels suggests a causal relationship between alloantibody and transplant rejection (5). Recently, Hourmant et al. also demonstrated that the presence of either DSA or NDSA significantly correlated with lower graft survival, poor transplant function and proteinuria (8). A 10-year follow-up of HLA and MICA antibodies in graft failure patients indicated that antibodies found in the peripheral circulation, which were not necessarily donor-specific, had a consistent association with graft failure and was in agreement with the causality hypothesis (9). Although it is reasonable that a patient develops antibodies against a mismatched donor antigen posttransplantation, the mechanism for the development of NDSA is not clear.

Pretransplant sensitization to nonself antigens usually results in a positive pretransplant PRA%, which might be a major source of NDSA. However, in this study, 18 out of 22 recipients with failed grafts that developed HLA-DR DSA had a negative pretransplant PRA%. Only three of these recipients (4, 6 & 17 in Table 1) had very low PRA and one of them (22) had a PRA of 95%. If we exclude these four recipients with pretransplant antibodies, the majority of the remaining ones developed NDSA. These data argue against a significant contribution for the pretransplant sensitization to nondonor antigen(s) as a major reason for NDSA development. Sequence-based antibody epitope mapping indicated that the majority of NDSA may share the same epitopes with mismatched donor antigens. These data suggest that in patients with failed grafts, who have detectable DSA, the majority of positive NDSA reactions detected by SA techniques are due to reactions of DSA against nondonor antigens that share amino acid(s) with donor antigens. In patients 10, 19, & 22 (last column of Table 2), we found that some of the NDSA, not sharing epitopes with DSA, shared common epitopes with each other. These data indicate that sensitization to nontransplant antigens pre- or posttransplantation can be the cause of the NDSA response. However, we could not rule out the possibility that other mechanisms may also be involved, such as nonspecific activation of NDSA response triggered by donor antigen immunization.

The concept of epitope sharing within HLA antigens was first proposed in the early 1980s when investigators found a significant number of monoclonal HLA antibodies that had polymorphic reactions against different HLA antigens (10–12). Allosera were also found to contain antibodies against shared (public) epitopes (13,14). Rodey et al. reported that 93 out of 103 antibody positive sera contained anti-public epitope antibodies whereas just 10 sera contained only antiprivate epitope antibodies (15). According to humoral theory of transplantation (1,7), allograft rejection can be mediated by antibodies; therefore, matching epitope that cause antibody response is more meaningful than matching HLA antigens (16,17). Nickerson's study clearly showed that matching for either private or public HLA epitopes reduces acute rejection episodes and improves 2-year renal allograft function (18). The identification of HLA antibody epitopes becomes very important to reduce humoral rejection and to prolong graft survival.

Protein sequence site-mutation by molecular biology techniques is a major approach to identify residues/epitopes that may play a critical role in protein–protein (e.g. antibody–antigen) or protein–DNA interactions. Even though site-mutation technique has also been used to map antibody epitopes in HLA research (19), comparison of differences in the amino acid sequences of a group of HLA alleles that are either recognized or not recognized by a monoclonal antibody or an alloserum is the most commonly used approach for potential HLA antibody epitope mapping (13,20). A recent breakthrough in HLA antibody research was the development of HLA SA beads (21). SA Flow or Luminex bead technology not only helps in the identification of antibody specificities but also helps in the identification of potential antibody epitopes. Because of the high polymorphism of the HLA antigens, any unique single amino acid residue or a combination of several amino acid residues may represent a potential immunogenic determinant if all the alleles with this residue (or residue combination) are positively targeted, while alleles without it are not recognized by testing antibody or serum. It should be noted that an antibody epitope identified by sequence comparison is only a 'potential' immunogenic determinant which may or may not be a real epitope. To prove that the potential epitope is real, further experimental steps need to be taken. Antibody absorption and elution from a combination of different SA beads or lines, each of which contain a unique epitope pattern, provides an ideal approach to further verify the identified potential epitopes (as in the examples in Figures 1 and 2). This new application of the SA technique may help to identify additional antibody epitopes that is responsible for alloantibody responses. According to the humoral theory (1,3), these epitopes are the key sequences that need to be matched for transplantation (16,17).

Another interesting finding of this study is the location of the potential epitopes. We found that 17 out of the 30 amino acid residues constituting potential antigenic determinants for alloantibodies are not present on the surface of the given DR antigen. The most distinct example is displayed in Figure 2. These findings imply that some polymorphic amino acid residues may be indirectly involved in antibody-antigen interactions by modifying the three-dimensional structure of the antigen or by selection of

peptides that can fit in the peptide binding groove (19,22). Since many of the identified potential donor antibody epitopes are not surface residues, we further investigated the correlation between antibody cytotoxicity and the location of epitopes. As shown in Table 2, 14 cytotoxicity positive sera for donor SA recombinant cell lines have at least one identified surface epitope. However, we could not identify any surface epitopes for four sera (2, 4, 12, &17) that have cytotoxic reactions against its donor specific antigen cell lines. A chi-square test reveals no correlation between antibody cytotoxicity and the presence of a surface epitope.

Based on this study, we reached the following conclusions: (1) the majority of the nondonor HLA antibody specificities detected in transplant recipients are due to sharing of the same epitope with donor antigen; (2) nonsurface amino acid residues might be involved in antibody/antigen interactions; (3)SA beads technique is a very useful experimental approach for the identification of potential antibody epitopes and (4) antibody absorption and elution with SA beads or cell lines represent a new means to further verify potential epitopes.

References

1. Terasaki PI. Humoral theory of transplantation. Am J Transplant 2003; 3: 665–673.
2. Terasaki PI, Ozawa M. Predicting kidney graft failure by HLA antibodies: A prospective trial. Am J Transplant 2004; 4: 438–444.
3. Terasaki PI, Cai J. Humoral theory of transplantation: Further evidence. Curr Opin Immunol 2005; 17: 541–545.
4. Terasaki PI, Ozawa M. Predictive value of HLA antibodies and serum creatinine in chronic rejection: Results of a 2-year prospective trial. Transplantation 2005; 80: 1194–1197.
5. Cai J, Terasaki PI, Bloom DD et al. Correlation between human leukocyte antigen antibody production and serum creatinine in patients receiving sirolimus monotherapy after Campath-1H induction. Transplantation 2004; 78: 919–924.
6. Cai J, Terasaki PI. Human leukocyte antigen antibodies for monitoring transplant patients. Surg Today 2005; 35: 605–612.
7. Cai J, Terasaki PI. Humoral theory of transplantation: Mechanism, prevention, and treatment. Hum Immunol 2005; 66: 334–342.
8. Hourmant M, Cesbron-Gautier A, Terasaki PI et al. Frequency and clinical implications of development of donor-specific and non-donor-specific HLA antibodies after kidney transplantation. J Am Soc Nephrol 2005; 16: 2804–2812.
9. Mizutani K, Terasaki P, Rosen A et al. Serial ten-year follow-up of HLA and MICA antibody production prior to kidney graft failure. Am J Transplant 2005; 5: 2265–2272.
10. McMichael AJ, Parham P, Rust N, Brodsky F. A monoclonal antibody that recognizes an antigenic determinant shared by HLA A2 and B17. Hum Immunol 1980; 1: 121–129.
11. Parham P, McLean J. Characterization, evolution, and molecular basis of a polymorphic antigenic determinant shared by HLA-A and B products. Hum Immunol 1980; 1: 131–139.
12. Igarashi M, Gebhard DH, Chen YX, Safai B, Evans RL, Ferrone S. Identification with the monoclonal antibody 26.163 of a determinant shared by the beta chains of the gene products of the HLA-DR, DQ, and DP loci. Hum Immunol 1986; 16: 347–355.
13. Piazza A, Poggi E, Ozzella G et al. Public epitope specificity of HLA class I antibodies induced by a failed kidney transplant: Alloantibody characterization by flow cytometric techniques. Transplantation 2006; 81: 1298–1305.
14. Zimmermann R, Wittmann G, Zingsem J, Blasczyk R, Weisbach V, Eckstein R. Antibodies to private and public HLA class I epitopes in platelet recipients. Transfusion 1999; 39: 772–780.
15. Rodey GE, Neylan JF, Whelchel JD, Revels KW, Bray RA. Epitope specificity of HLA class I alloantibodies. I. Frequency analysis of antibodies to private versus public specificities in potential transplant recipients. Hum Immunol 1994; 39: 272–282.
16. Terasaki PI, Park MS, Takemoto S et al. Overview and epitope matching. Clin Transpl 1989; 499–516.
17. Terasaki PI, Takemoto S, Park MS, Clark B. Landsteiner award. HLA epitope matching. Transfusion 1992; 32: 775–786.
18. McKennaRM, Lee KR, Gough JC et al. Matching for private or public HLA epitopes reduces acute rejection episodes and improves two-year renal allograft function. Transplantation 1998; 66: 38–43.
19. Drover S, Marshall WH, Kwok WW, Nepom GT, Karr RW. Amino acids in the peptide-binding groove influence an antibody-defined, disease-associated HLA-DR epitope. Scand J Immunol 1994; 39: 539–550.
20. Seitz C, Uchanska-Ziegler B, Zank A, Ziegler A. The monoclonal antibody HCA2 recognises a broadly shared epitope on selected classical as well as several non-classical HLA class I molecules. Mol Immunol 1998; 35: 819–827.
21. Pei R, Lee JH, Shih NJ, Chen M, Terasaki PI. Single human leukocyte antigen flow cytometry beads for accurate identification of human leukocyte antigen antibody specificities. Transplantation 2003; 75: 43–49.
22. Ge J, Bratlie A, Hannestad K. A human hybridoma monoclonal antibody (TrJ11) recognizing a new HLA-DR epitope shared by DR4, DR8, DR11, and DRB1∗1303. Hum Immunol 1995; 42: 27–34.