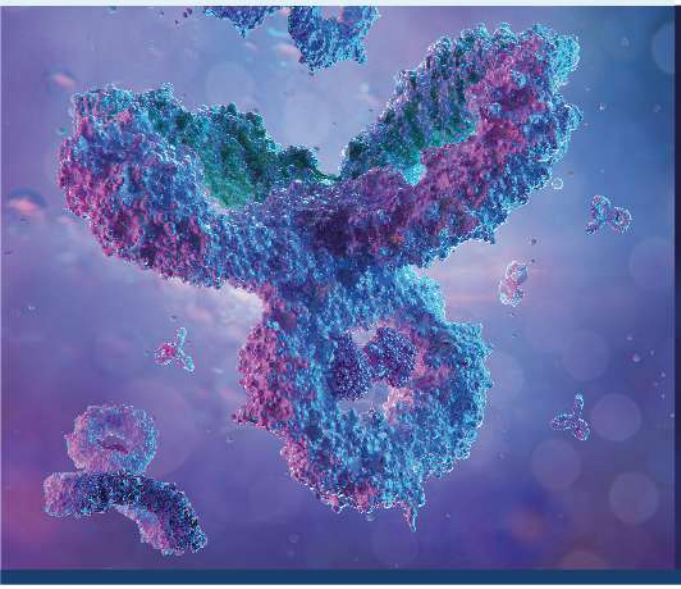


HIGHLIGHTS OF THE CASE

Implementation of Epitope matching/PIRCHE reduces immunogenicity and denovo donor specific antibodies: a strategy for better molecular matching in transplantation.

Case 1:

CLINICAL FINDINGS

Patient HLA types:

Locus	HLA-A*	HLA-B*	HLA-C*	HLA-DRB1*	HLA-DQB1*
Allele 1	A* 26:01:01	B* 08:01:01	C* 07:01:01	DRB1* 03:01:01	DQB1* 02:01:01
Allele 2	A* 33:03:01	B* 44:03:02	C* 07:02:01	DRB1* 07:01:01	DQB1* 02:01:01

Donor HLA types:

Locus	HLA-A*	HLA-B*	HLA-C*	HLA-DRB1*	HLA-DQB1*
Allele 1	A* 03:01:01	B* 08:01:01	C* 07:01:01	DRB1* 03:01:01	DQB1* 02:01:01
Allele 2	A* 26:01:01	B* 44:03:02	C* 07:02:01	DRB1* 07:01:01	DQB1* 02:01:01

SAB antibody reactivity were observed with marginal positive for:

DQ6 (MFI=1043, 935) and **DQ5** (MFI=882, 865)

Molecular alleles: DQB1*06:04 | DQB1*06:02 | DQB1*05:02 | DQB1*06:03 | DQB1*06:01 | DQB1*05:03 | DQB1*06:01

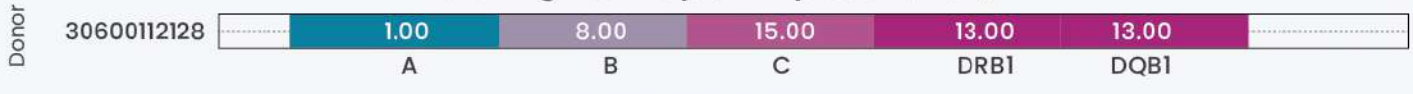
ANALYSIS

PIRCHE and HLA eplet registry confirms the presence high reactive antibodies for donor DQB1 alleles

PIRCHE Heat map on antibody reactivity

Patient/Donor ID	A	B	C	DRB1	DQB1	PIRCHE II
30600112124	01:01:01:01 11:01:01:01	51:06:01:01 56:01:01:02	01:02:01:01 14:02:01:01	04:03:01:03 15:02:01:03	03:02:01:01 06:01:01:01	
30600112128	01:01:01:01 30:01:01:01	13:02:01:01 15:02:01:01	06:02:01:01 08:01:01:01	07:01:01:04 12:02:01:05	02:02:01:01 03:01:01:07	50.00

Matching heatmap (DRB1 presentation)



Mismatch calculator in epitope registry:

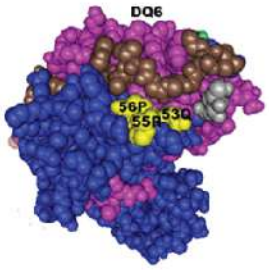
Donor/Immunizer Vs. Patient 1	A/B/C	DRB1/3/4/5	DQA1/DQB1	DPA/DPB1	MICA	TOTAL
	23	9	14			46

HLA LOCI GROUP	MISMATCHES QTY.	MISMATCHES DETAILS
A/B/C	23	All mismatches: 9F, [44RT], [62QE], 71QS, 76VDT, 77D, [80I], 95W, 97I, 97T, 105S, 114R, [144K], [144KR], [149AH, [150AAH], 152RE, [161N], [163LW], 170RH, 184H, [193PV], 275EL Single-allele mismatch load : **A*03:01** 14 **A*26:01** 0 **B*08:01** 0 **B*52:01** 8 **C*07:02** 0 **C*12:02** 3
DRB1/3/4/5	9	All mismatches: 37S, 70QA, [70QT], 71A, [73A], 74A, 77TY, 96Q, [142M] Single-allele mismatch load: **DRB1*03:01** 0 **DRB1*15:02** 9
DQA1/DQB1	14	All mismatches: 3P, [45GV], [46VY], [52PQ], [55R], 55RPD, 56PD, 70RT, 74EL, [77T], 86A, [87F], 125G, 167H Single-allele mismatch load: **DQB1*02:01** 0 **DQB1*06:01** 14
DPA/DPB1		Results omitted because donor/immunizer and patient were not typed for this HLA locus
MICA		Results omitted because donor/immunizer and patient were not typed for this HLA locus

VERIFIED ANTIBODY REPORT: THE EPLET 55R PRESENT IN DQB1*06:01 EXHIBITED HIGH REACTIVITY. IN ADDITION EPLET 53Q AND 56P PRESENT IN THE CORE PEPTIDE OF ANTIGEN RECOGNITION DOMAIN ADDS THE IMMUNOGENICITY

Example of an SAB assay of a pregnancy serum provided by Stefan Schaub (Basel, Switzerland) with 55R-reactive DQB antibodies

Pregnancy Mother Case #164 Child	DQB1*03:01 DQB1*03:01 DQB1*06:02 DQA1*01:02	DQA1*03:05 DQA1*05:01	
Prep DQB	DQA	DQBep	MFI
60 DQB1*06:02	DQA*01:02 IMM	55R	9526
59 DQB1*06:02	DQA*01:01 MM	55R	11662
63 DQB1*06:09	DQA*01:02	55R	14239
62 DQB1*06:04	DQA*01:02	55R	13760
61 DQB1*06:03	DQA*01:03	55R	12963
58 DQB1*06:01	DQA*01:03	55R	13085
56 DQB1*05:01	DQA*01:01	55R	11206
57 DQB1*05:02	DQA*01:02	55R	10569
54 DQB1*04:02	DQA*02:01	55R	7212
55 DQB1*04:02	DQA*04:01	55R	8165
53 DQB1*04:01	DQA*03:03	55R	10547
52 DQB1*04:01	DQA*02:01	55R	6729
Other DQ dimers (N=17)			215+226



Certain 55R-specific antibodies exhibit two reactivity patterns (see below). The group of 55R-carrying DQ5 and DQ6 alleles with higher MFI values carry the 53Q and 56P residues. In contrast, the 53L and 56L carrying DQ4 alleles have significantly lower MFI values

CONCLUSION

The DQ6 and DQ5 serological HLA alleles, DQB1*06:01 which is present in the donor HLA allele will evoke immunogenicity with recipient T/B cells.