

Enhancing the

Transplant Success

WITH EPITOPE MATCHING IN
HLA TYPING

- HLA antibodies are primary causes of allograft rejection and transplant failures.
- Antibodies recognize structurally defined epitopes in which so-called eplets play a dominant role.
- Eplets are key components of epitope-based class I and class II HLA matching.



Clinical Utility

- HLA matching at the epitope level is a crucial analysis in organ transplantation.
- Epitope analysis of serum HLA antibodies is the most efficient approach to identify transplant donors for sensitized patients.
- HLA mismatches with low eplet loads are preferable donors.
- Avoid grafts from donors with of high immunogenic eplets.

CASE STUDY

Implementation of Epitope matching/PIRCHE reduces immunogenicity and denovo donor specific antibodies:

A Strategy for better Molecular Matching in Transplantation

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 few DQ6 (MFI=1043, 935) and DQ5 (MFI=882, 865) allele groups
 SAB positive molecular alleles: DQB1*06:04, DQB1*06:02, DQB1*05:02, DQB1*06:03, DQB1*06:01, DQB1*05:03, DQB1*06:01

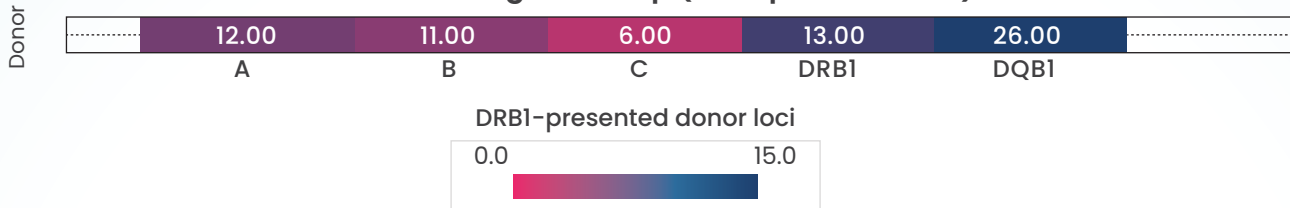
ANALYSIS

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
000	26:01:01 33:03:01	08:01:01 44:03:02	07:01:01 07:02:01	03:01:01 07:01:01	02:01:01 02:01:01	
000	03:01:01 26:01:01	08:01:01 52:01:01	07:02:01 12:02:01	03:01:01 15:02:02	02:01:01 06:01:01	68.00

Matching heatmap (DRB1 presentation)



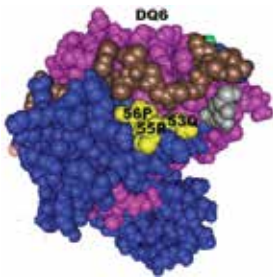
Mismatch calculator in epitope registry:

Donor/Immunizer Vs. Patient 1		A/B/C	DRB1/3/4/5	DQA1/DQB1	DPA/DPB1	MICA	TOTAL
		20	9	14			43
HLA LOCI GROUP	MISMATCHES OTY.	MISMATCHES DETAILS					
A/B/C	20	All mismatches : 9F, [44RT], [62QE], 71QS, [80], 95W, 97I, 97T, 114R, [144K], [144KR], 149AH, [150AAH], 152RE, [161D], [163LW], 170RH, 184H, [193PV], 275EL Single-allele mismatch load : A*03:01 14 A*26:01 0 B*52:01 0 B*08:01 0 C*12:02 3 C*07:02 0					
DRB1/3/4/5	9	All mismatches: 37S, 70QA, [70QT], 71A, [73A], 74A, 77TY, 96Q, [142M] Single-allele mismatch load: DRB1*15:02 9 DRB1*03:01 0					
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 Case #	Mother Child	DQB1*03:01	DQB1*03:01	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

DQB1*06:01 which is present in the donor HLA allele will evoke immunogenicity with recipient T/B cells.

Test Ordering Information:

Test code	Test Name	Components	Specimen Type	Methodology	Test Schedule & TAT
H0015ae	HLA typing A, B, C, DRB1, DQB1 loci Class I & II (NGS) + Epitope matching	Class I&II + Epitope matching	2ml peripheral blood, saliva, swab, DBS in EDTA tube	NGS	Sample by Thursday & Monday and Report on Monday & Friday
H0015af	HLA typing A, B, C, DRB1, DQB1, DPB1 loci Class I & II (NGS) + Epitope matching	Class I&II + Epitope matching			
H0015e	HLA typing A, B, C, DRB1, DQB1 loci Class I & II (NGS)	A, B, C, DRB1, DQB1			
H0015aa	HLA typing A, B, C, DRB1, DQB1, DPB1 loci Class I & II (NGS)	A, B, C, DRB1, DQB1, DPB1			