Precision in Post-Transplant Management: Revealing Epitope Mismatch Analysis for Enhanced Graft Survival Prediction

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INTRODUCTION

- The Human Leukocyte Antigens (HLA) are a family of genes that encode cell surface proteins critical in immune recognition and response.
- Mismatch between patient and donor HLA alleles confer a risk of graft rejection, even with immunosuppression.
- Immunosuppressant side effects include cancer and infection, creating demand for personalized dosing to minimize harm.

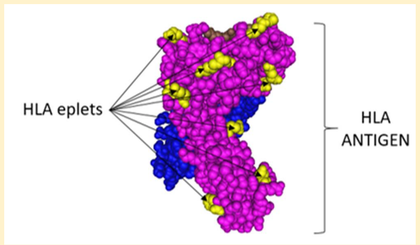


Fig. 1. Eplets are short amino acid sequences situated on the surface of HLA molecules essential to antibody recognition of HLA.

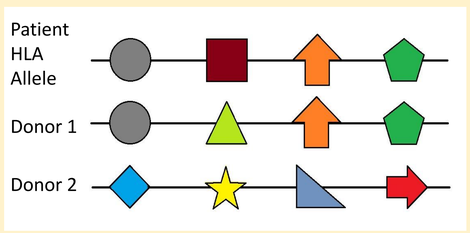


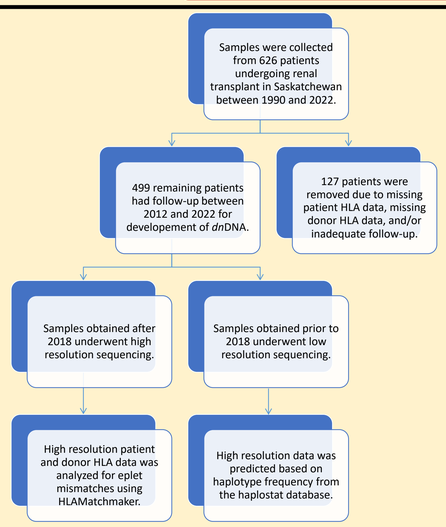
Fig. 2. The patient antigen is mismatched with that of both donors. However, Donor 2 has 4 eplet mismatches with the patient compared to only 1 mismatch for Donor 1.

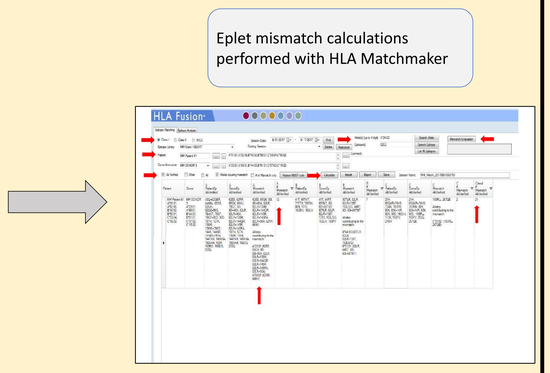
- We hypothesize the patient would be at lower risk of rejection if transplanted with a donor organ with less eplet mismatches.

OBJECTIVES

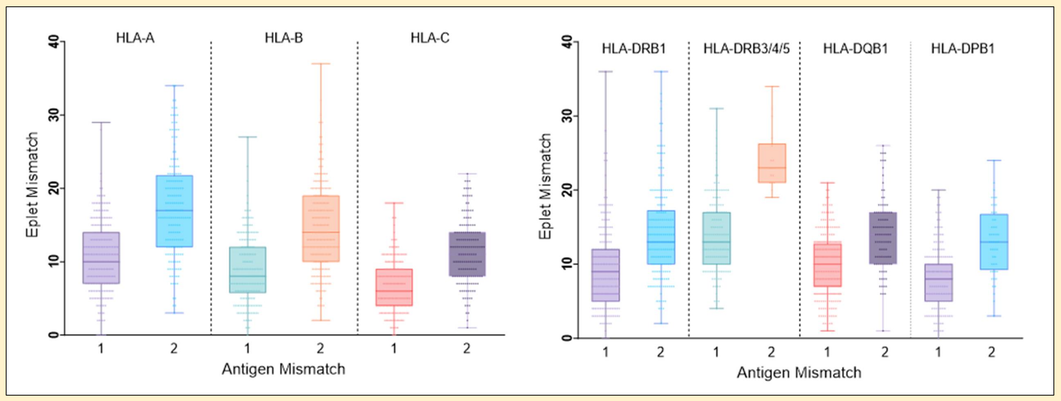
- Assess the association between patient-donor eplet mismatch and graft rejection measured by *dn*DSA formation.
- Determine risk-based eplet mismatch cutoffs to guide post-transplant management.

METHODS





RESULTS



- **Fig. 3.** Comparison of the population eplet and whole antigen mismatch. Notably at most HLA loci, there is great variability in the eplet mismatch within the same antigen mismatch group.

Patient Characteristics	Patients With class specific *dn*DSA	Patients Without dnDSA	P Value
Recipient Age	51	54	0.0648
Recipient Gender, % Female	47.73%	37.32%	0.0723
Living Donor, %	36%	33%	0.4871
First Transplant, %	95%	95%	0.8222
Recipient Ethnicity, % Caucasian	64%	76%	0.0001
Recipient Ethnicity, % First Nations	25%	14%	0.0001
Recipient Ethnicity, % Other	11%	10%	0.6274
HLA-A Antigen Mismatch	1.3	1.1	0.3235
HLA-B Antigen Mismatch	1.9	1.4	0.0158
HLA-C Antigen Mismatch	1.7	1.2	0.0788
HLA-DR1 Antigen Mismatch	1.3	1.2	0.7258
HLA-DR345 Antigen Mismatch	1.1	0.5	0.0009
HLA-DQ Antigen Mismatch	1.2	0.9	0.0013
HLA-DP Antigen Mismatch	1	0.8	0.5366
HLA-A Eplet Mismatch	15.6	10.7	0.0064
HLA-B Eplet Mismatch	15.3	10.6	0.0318
HLA-C Eplet Mismatch	12	7.1	0.0215
HLA-DR1 Eplet Mismatch	11.4	9.6	0.4771
HLA-DR345 Eplet Mismatch	16.2	7.5	0.0004
HLA-DQ Eplet Mismatch	11.4	7.9	0.0001
HLA-DP Eplet Mismatch	8.6	6.7	0.4514

Table 1. Demographics table of patients with and without development of *dn*DSA.

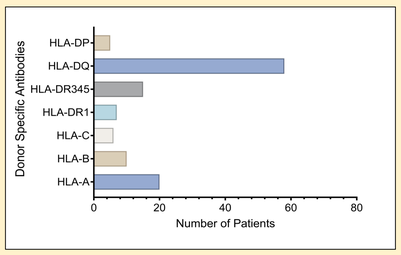


Fig. 4. Number of patients that developed *dn*DSA toward each HLA loci.

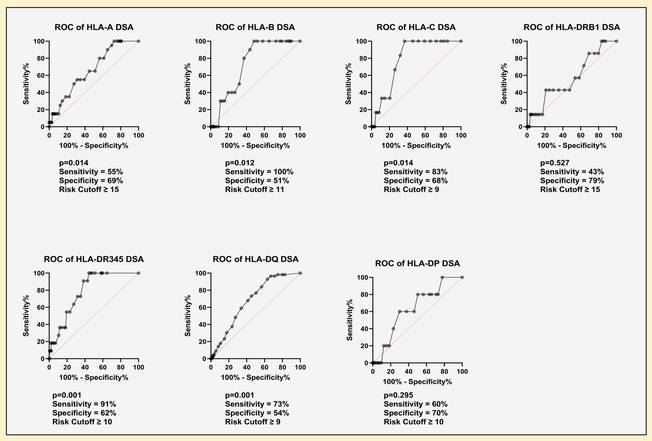


Fig. 5. The high-risk cutoff values for eplet mismatch count were determined by ROC analysis. Significant values were found for HLA A, B, C, DR3/4/5 and DQ. Sensitivity and specificity are listed above alongside cutoff values.

RESULTS

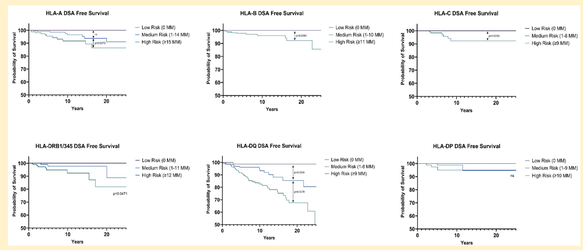


Fig. 6. Kaplan-Meier survival analysis confirmed these findings and revealed a significant difference in DSA-free survival between risk-stratified groups (5%, 3%, 10% at 10 years, $p<0.05$).

CONCLUSION & DISCUSSION

- We demonstrated the variability of eplet mismatches within patients who have the same number of antigen mismatches.
- The number of eplet mismatches at HLA A, B, C, DR3/4/5, and DQ loci was found to correlate positively with loci specific *dn*DSA formation.
- Optimized eplet mismatch cutoffs (Figure 5) were determined for risk stratification and to aid in clinical decision making.
- Our future works will further examine the relationship between eplet mismatch and clinical rejection through:
  - Tacrolimus titers
  - Biopsy findings
- We aim to determine appropriate eplet mismatch thresholds to guide tacrolimus dosing while minimizing the risk of rejection
- Furthermore, we hope to integrate clinical data to further improve matching and better predict patient prognosis post-transplant.

ACKNOWLEDGEMENTS

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