Population Analysis of HLA Eplet and Allele Frequencies to Assess the Feasibility of Eplet-Matching in Canada

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INTRODUCTION

- Antibody-mediated rejection (AMR) is a leading cause of long-term kidney transplant failures¹
- Kidney patients and donors matched at their histocompatibility human leukocyte antigen (HLA) genes are associated with lower AMR risk²
- There are >20,000 HLA alleles, making it difficult to match²
- Antibodies recognize and bind to eplets, clusters of amino acids on HLA²
- “Eplet-matching” is a more precise and biologically-relevant matching tool
- There are far fewer eplets than alleles: potentially making eplet-matching feasible in Canada³

Fig 1. Ribbon diagram of the top-down view of HLA protein A*01:01. Eplets are highlighted in red.

AIM

This study describes HLA allele and eplet frequencies in kidney patient and donor populations in BC to compare the likelihood of matching by each method.

MATERIALS AND METHODS

RESULTS

1,846 patients and donors were included in the study population

- 438 transplanted patients (KTx)
- 554 potential living donors (LD)
- 611 pre-transplant patients (KPre)
- 243 deceased donors (DD)

Allele relative frequencies occur at lower values than eplets

- Allele relative frequencies medians: 0.004 – 0.023
- Eplet relative frequencies medians: 0.429 – 0.509
- Majority of allele relative frequencies were <0.10

RESULTS

Clusters of subjects were grouped into three distinct eplet patterns, the HLA epitope

- Using k-means clustering, three clusters were identified in the total study sample for both class I and class II
- Each cluster represents a pattern of eplets predominant in individuals in their relevant cluster

Fig 4. Cluster analysis for class II HLA eplets in the total study population. Eplets that are predominant in their respective cluster are boxed in red. Frequent eplets are coloured red, while rare eplets are blue.

Subjects segregate into different epitope clusters with distinct frequencies

- The relative frequency of each cluster in the patient and donor groups were determined
- Clusters are dependent on the patient/donor group for HLA class I (p-value < 0.001) but independent for class II (p-value = 0.237).
- Cluster 1 of class I is smaller in the transplant (KPre, KTx) than in the donor (DD, LD) cohorts. The eplets 76ANT, 44KM3, 163RG, unique to cluster 1, are mostly contributed by alleles A*01:01, A*01:02.

Fig 5. The frequency of clusters for class I (left) and class II (right) in the patient and donor groups.

CONCLUSION

- Conversion of alleles to eplets result in a significant reduction in HLA complexity
- Kidney patient and donor populations share common eplets with similar eplet frequencies
- HLA epitope frequencies vary between the cohorts for class I but not for class II
- Overall, the results support the use of eplets in histocompatibility matching for improving long-term transplant outcomes

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