Different serotypes among DQB1*05 alleles: DQB1*05:01, DQB1*05:02, and DQB1*05:03

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BACKGROUND and AIM

The serotypes among different alleles of a parental HLA antigen may be different. Confirmation of serotype of corresponding allele is critical to analyze the donor-specific antibody (DSA). The current study was to explore the difference of allele-specific reactivity of HLA-DQ5 and to study the three potential serotypes corresponding to DQ5 alleles: DQB1*05:01, DQB1*05:02 and DQB1*05:03.

METHODS

We retrospectively reviewed the HLA antibody tests performed in our center in the past three years and identified patients who showed DQ5 reactivities. For these patients, we conducted high resolution typing, PRA phenotype beads assay, and ExPlex kit to study the reactivities among three allele-specific reactivity for DQB1*05:01, DQB1*05:01 and DQB1*05:03.

RESULTS

Per OPTN cPRA calculator, DQ5 is present in 31% population, in which DQB1*05:01 accounts for 22%, DQB1*05:02 for 4% and DQB1*05:03 for 5%, respectively. In our DSA analysis, we encountered cases of donor carrying DQB1*05:03 but we could not determine if there is a DSA using the current HLA SAB assay (due to the absence of DQB1*05:03 detecting bead). Scenario 1: a kidney candidate typed HLA-DQ5 showed strong allele-specific reactivity for DQB1*05:01 (MFI>25K), moderate/low reactivity DQB1*05:02 (MFI~2.5K), and unknown reactivity for DQB1*05:03. We performed high-resolution HLA typing and revealed that patient carries DQB1*05:03. ExPlex assay and PRA phenotype bead assay were further performed and both assays showed that DQB1*05:03 was negative (Figure 1). This patient received offered donors with DQ5, when a donor typed DQB1*05:03, it was considered as a match on DQB1 locus, instead of reporting DQ5 DSA. Scenario 2: a heart candidate typed HLA-DQ5 (possible allele DQB1*05:01) showed moderate/low reactivity of DQB1*05:02 (MFI~2.5K), negative DQB1*05:01 and unknown reactivity for DQB1*05:03. ExPlex assay and PRA phenotype bead assays showed DQB1*05:03 was negative (Figure 2). Alignment study for the gene and protein sequence revealed that the key determinant amino acid among the allele DQB1*05:01, DQB1*05:02, and DQB1*05:03 is the 57VSD epitope, in which one amino acid difference change the antibody specificity (Figure 3 and 4).

Figure 1. DQB1*05:01 antibody does react with DQB1*05:03 single antigen bead

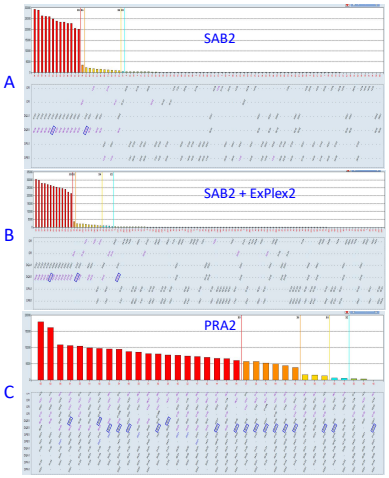

Figure 2: DQB1*05:02 antibody does react with DQB1*05:01 or DQB1*05:03 single antigen beads

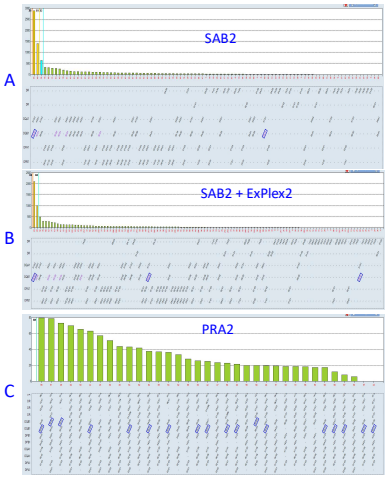

Figure 3. 57 VSD epitope determine allele-specific serotype of DQB1*05:01, DQB1*05:01, DQB1*05:03

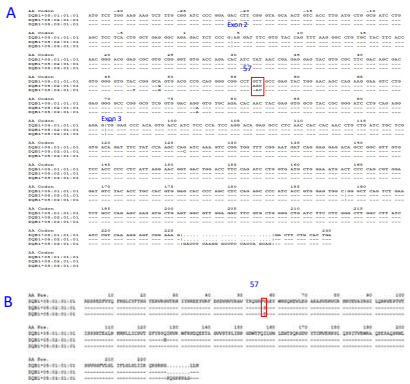

Figure 4. Structural location of 57 VSD epitope

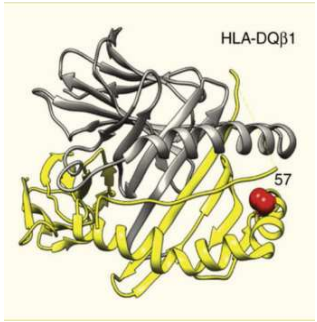

Photo abstracted from book edited by MJ Redondo et al https://www.ncbi.nlm.nih.gov/books/NBK597411/

CONCLUSION

The DQB1*05:01, DQB1*05:02 and DQB1*05:03 alleles appear to have their own distinguishable serotype. Determining and differentiating the serological reactivity among different allele is helpful to define the DSA and may impact the clinical decision.

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