A MULTICENTER ANALYSIS OF THE PROPORTION AND PATTERN OF UNEXPLAINED HLA ANTIBODIES IN KIDNEY RECIPIENTS WITHOUT A HISTORY OF SENSITIZATION

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Background: Previous studies report a high prevalence of unexplained antibody reactivities on the SAB test. In a contemporary multicenter cohort of non-sensitized kidney recipients, our study objective was to analyze the proportion and pattern of unexplained HLA antibodies on the single antigen bead (SAB) test and to quantify their impact on access to transplant.

Study cohort: OL SAB data from 285 non-sensitized kidney recipients (non-transfused males and non-transfused, nulliparous females) from 3 US-Canadian centers (center 1: n=209; center 2; n=42; center 3: n=34) were analyzed. Centers 1 and 2 utilized comparable SAB reagents/protocols, enabling comparison of the proportion of patients with HLA reactivities based on MFI threshold >1000. The proportion of patients with director-defined unacceptable antigens and their associated cPRA was examined in all 3 centers.

Results: The majority of patients (n=202/251) had evidence of at least 1 reactivity on the OL SAB test based on MFI threshold >1000 (HLA-A: 13.3%, B: 17.9%, C: 8.1%, DR: 19.6%, DQ: 17.4%, DP: 23.7%), with 23% (n=47/202) having a single, and the remaining having multiple antibodies. Unsupervised machine clustering using nonnegative matrix factorization identified distinct reactivity patterns in class I and II (Figure 1), some of which were shared between patients from different centers. Despite similarities in MFI-defined HLA specificities, significant differences were observed in the determination of unacceptable antigens between centers, leading to a differential impact on access to transplant (Table 1).

Conclusions: The majority of non-sensitized kidney recipients showed evidence of unexplained reactivities on the SAB test which can affect access to transplant. Further work is required to determine the etiology and relevance of spurious HLA reactivities not explained by clinical history.

Site	Total number of patients (n)	Number of patients with least one antibody based on MFI >1000 (n, %)	Number of patients with director-defined unacceptable antigens (n, %)	cPRA based on unacceptable antigens (median, IQR)
Center 1	209	173 (85.6%)	137 (65.6%)	26.3 (39.6)
Center 2	42	29 (69.0%)	2 (4.8%)	44.5 (17.0)
Center 3	34	N/A*	16 (47.1%)	2.93 (16.3)
Total	285	202 (80.5%)	155 (54.4%)	23.22 (40.4)

Table 1. Number and proportion of non-sensitized patients with unexplained antibodies based on MFI threshold and director interpretation. cPRA was calculated based on director-defined unacceptable antigens. *Center 3 not included due to use of a different SAB reagent/protocol.

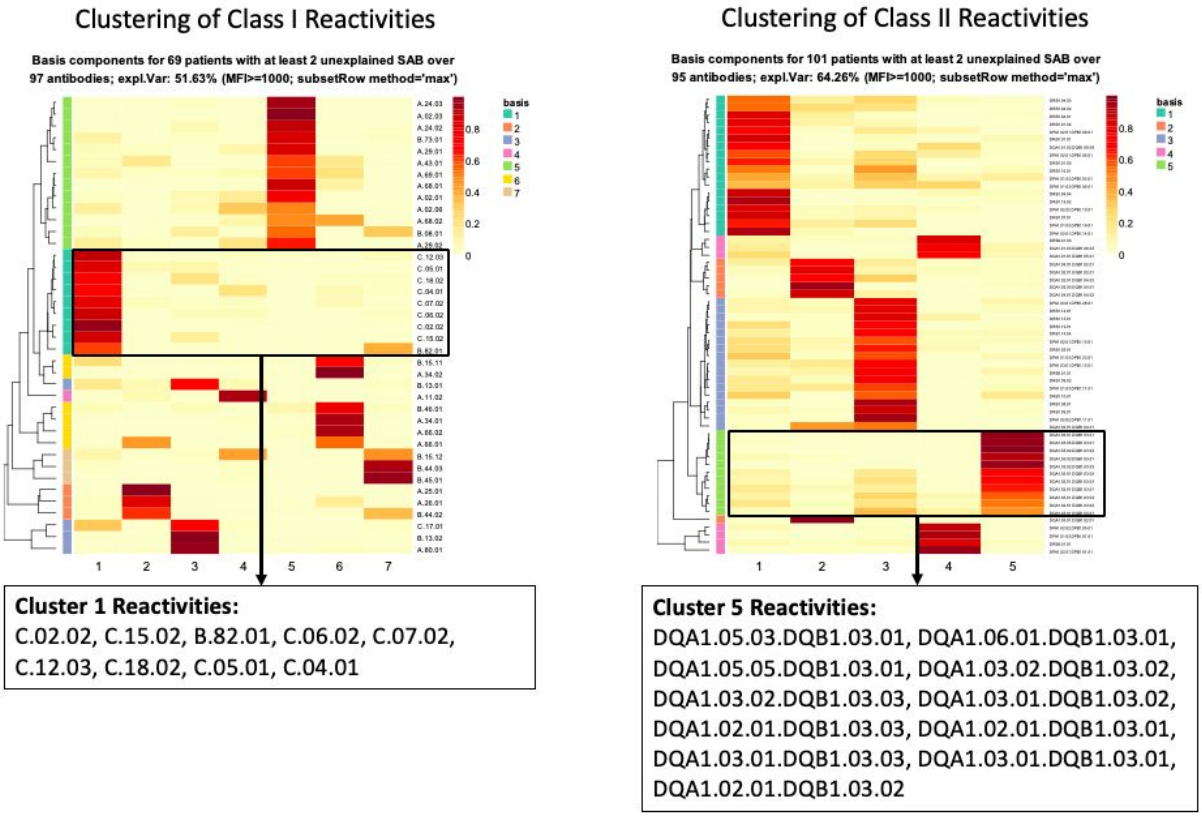

Figure 1. Unsupervised machine clustering of unexplained class I and II reactivities.