IMMUCOR

# FEATURED PUBLICATION

"Highly sensitized patients awaiting deceased donor renal transplants are disadvantaged by the presence of denatured HLA antibody detected in routine HLA antibody testing." *

The authors present data to suggest that the use of the Immucor assay to adjudicate unacceptable antigens in highly sensitized patients can accelerate time to transplant

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ORIGINAL ARTICLE

HLA Immune Response Genetics WILEY

## Highly sensitised patients awaiting deceased donor renal transplants are disadvantaged by the presence of denatured HLA antibody detected in routine HLA antibody testing

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Luminex single antigen bead (SAB) assays used to detect HLA antibodies may artificially increase sensitisation in highly sensitised patients (HSP). The presence of denatured HLA (dHLA) within the assay enables antibodies specific to cryptic HLA epitopes to bind, such antibodies are not clinically relevant. We sought to exclude dHLA reactivity in a cohort of very HSP, calculated reaction frequency (cRF) 95%–100% and determine the effect upon sensitisation. Such patients have limited access to suitable donors and small changes in their HLA antibody profile, particularly where their cRF is 100%, can increase their opportunity of a transplant. We determined the presence of dHLA by aligning antibody reactivity which did not correspond to known HLA class I epitope mismatches with the results of assays modified to detect class I dHLA. 130 class I dHLA reactions were identified within 11 HSP, all of whom had clear sensitising events. cRF was corrected for dHLA, mean cRF 98.2% (93–100) pre and 95.5% (87–100) post correction ($p = 0.0156$). An increase in the number of predicted compatible donors ($p = 0.0078$) after dHLA correction was demonstrated. Two manufacturers SAB assays were used. A reduction of patients with 100% cRF was observed for both manufactures. dHLA is contributing to sensitisation in HSP and is detrimental to their chances of receiving a compatible transplant. The observed dHLA reactivity varied according to kit manufacturers ($p = 0.0001$), this is potentially a useful finding for laboratories wishing to discriminate between nHLA and dHLA, but without the resources required to regularly perform dHLA assay and epitope analyses.

**KEYWORDS**
denatured HLA, highly sensitised patients, HLA antibodies

### 1 | INTRODUCTION

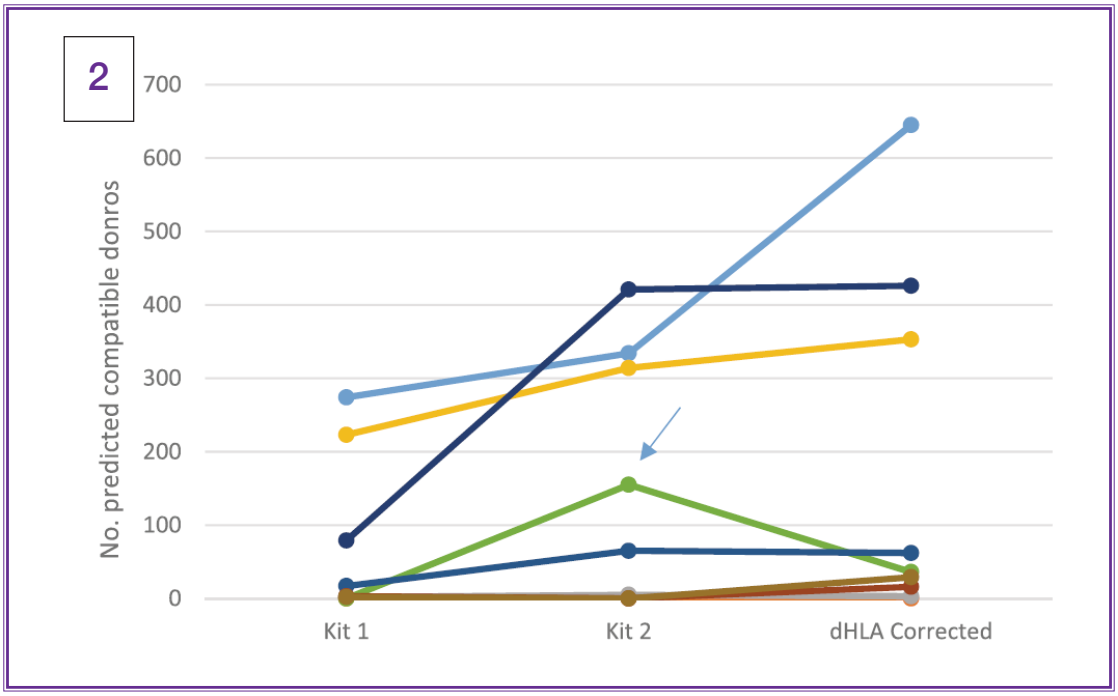
The association of donor-specific HLA antibodies (HLA-DSA) with graft loss and poor outcomes in renal transplantation is well documented.[1–3] This association has led to the pre-emptive avoidance of HLA-DSA in patients

**Abbreviations:** CIT, cold Ischemia time; cRF, calculated reaction frequency; dHLA, denatured HLA; HLA-DSA, donor specific HLA antibodies; HSP, highly sensitised patients; nHLA, native confirmation HLA; SAB, single antigen beads; vXM, virtual crossmatch; β-2m, β-2microglobulin.

*Battle, RK, Rennie, TJW, Phelan, PJ, Abel, AA, McConnell, S, Turner, DM. Highly sensitised patients awaiting deceased donor renal transplants are disadvantaged by the presence of denatured HLA antibody detected in routine HLA antibody testing. HLA. 2022; 100( 1): 24- 36. doi:10.1111/tan.14578

## How do false positive results impact access/allocation?




| *Assay type* | Mean cRF | Mean Predicted donor no |
|---|---|---|
| *Kit 1* | 98.2% (93-100) | 60.2 (0-645) |
| *Kit 2* | 96.5% (91-100) | 149 (0-421) |
| *dHLA corrected* | 95.5 (84-100) ***P=0.0156*** | 149 (0-645) ***P=0.0078*** |

**Kit 1**= Other Vendor

**Kit 2** = LIFECODES

**dHLA Corrected** = # of donors after removal of denatured HLA reactivity

Battle et al. (2022). HLA. 2022;100:24–36

## A SUMMARY OF THE BATTLE ET AL. (2021) PAPER STATES THAT*:

- "Given the lower impact of dHLA described within Kit 2 (Immucor), one potential way of managing these patients is to use both Kit 1 and Kit 2 for determining what HLA antigens should be declared as unacceptable with centralized organ allocation registries, particularly in Highly Sensitized Patients."

- "We suggest comparing the results of Kit 1 and 2 when assigning unacceptable antigens with a central registry for cadaveric organ allocation. Such an approach would be easier to implement into a routine laboratory than performing dHLA assays."

- "Our data suggest this (the use of Kit 1 and 2 to assign unacceptable) would reduce the impact of dHLA and result in patients' numbers of potential compatible donors to increase, and consequently their chances of receiving an offer of a deceased donor kidney would also increase."

*Battle, RK, Rennie, TJW, Phelan, PJ, Abel, AA, McConnell, S, Turner, DM. Highly sensitised patients awaiting deceased donor renal transplants are disadvantaged by the presence of denatured HLA antibody detected in routine HLA antibody testing. HLA. 2022; 100( 1): 24- 36. doi:10.1111/tan.14578