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The Clinical Significance of HLA-DP mismatches in kidney Transplantations

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Background: HLA–DP is considered to be less immunogenic than other HLA antigens because of low expression on renal endothelium. The evidence for this is however scarce.

Methods: We evaluated the clinical significance of HLA-DP MM in kidney transplantations in 3 multicentre cohorts. In the 1st large cohort, we evaluated the prevalence of HLA-DP antibodies (Abs) in patients (pts) who experienced 1 or more graft failures (2008–2018; N=497). A 2nd cohort was composed of pts with only HLA-DP DSA (2008–2018; N=14). In this optimally selected cohort (no interference by other DSA) clinical outcome was evaluated, including histologic evaluation of biopsies by the Banff criteria. In the 3rd cohort (N=100), the role of CDC-XM/FCXM in clinical decision-making was examined by collecting XM data from donor-patient pairs with only HLA-DP DSA.

Results: In the 1st cohort, DP Abs were detected in 99 cases (20%) and DQ Abs in 266 cases (54%). In 80%, DP Abs appeared only after graft failure. In the cohort of pts who had only DP DSA, AMR occurred in 5/14 pts (36%). In all 5 cases, DSA MFI was $\geq$3141 but with negative CDC-XM. None of the pts with lower MFI DP-DSA experienced AMR. Epitope analysis showed an association with immunodominant eplets 84DEAV/85GPM-56AE/EE. In the non-AMR group (9/14) these eplets were also present as a MM but only in the presence of DSA with low MFI. Interestingly, we also observed high MFI (MFI>20.000) DSA against the DPA locus (not DPB) in the non-AMR group. When we evaluated the XM results of cases with only DP DSA, a positive XM was only observed in case immunodominant eplets were present and MFI was $\geq$14.050 (CDC-XM) or $\geq$3616 (FCXM). DSA against the DPA locus only, even up to MFI 14.233, never led to positive FCXM results.

Conclusions: AMR was observed in all cases with HLA-DP DSA when MFI$\geq$3141 and directed towards immunodominant eplets. This illustrates that when HLA-DP Abs are found, HLA-DP typing, epitope analysis and FCXM are indicated for optimal decision-making.