Title: Gene expression profiling in patients with Antibody Mediated Rejection

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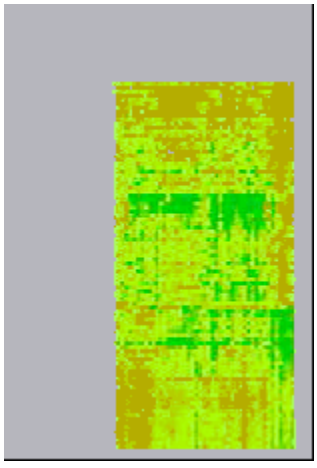
Purpose: Antibody mediated Rejection (AMR) is associated with poor outcome. We hypothesized that specific gene expression profiles may be present in patients with AMR.

Methods and Materials: Based on the Columbia University cohort from the CARGO study, we analyzed PBMC gene microarrays from patients meeting criteria for AMR by using SAM, Gene ontology analysis and hierarchical clustering. A FDR<5-10% was considered significant.

Results: Five patients fulfilled criteria for AMR. We found dramatic changes in the expression profile sand coherent enrichment of gene ontology categories. Represented genes included BCL11A (leukemia and B-Cell lymphomas), BNIP3L (suppression of cell proliferation), AGPTA1, HLA-DRA, CD1D and CD74 (MHC-related); FADD (apoptosis), TNFRSF25 and TNFRSF10 (T cell development); GZMB (target cell apoptosis),IGHG-1, 4 (immunoglobulin chains), IGLL1 (cellular proliferation and differentiation), IL1R2 (inhibits the activity of its ligands), IL-4 (antagonize IL-1), IL7R (differentiation and activation of T cells), IRF4 (B-cell proliferation and differentiation, T-Cell differentiation and induction of IL-10 and IL-2), ITK (T-cell kinase containing SH2 and SH3), OSM (regulates IL-6, G-CSF and GM-CSF in endothelial cells), PTPRC (regulates T- and B-cell antigen receptor signaling in hematopoietic cells) and TNFAIP6 (induced in vascular smooth muscle). The figure show high correlation in patients with AMR (right).



Conclusions: Patients suffering AMR have specific gene expression profiles involving several B-cell but also T-Cell-related genes. These results should encourage the design of future studies aimed to dissect the cross-talk between the different known forms of rejection