Non-invasive diagnosis for acute rejection using blood mRNA signature reflecting allograft status in kidney transplantation

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Background: Despite improvements in immunosuppressive therapy over the years, acute rejection (AR) episodes that required treatment are still a significant risk factor for poor graft outcomes. Monitoring renal graft status through peripheral blood (PB) rather than invasive biopsy could reduce bleeding risk and costs.

Methods: Blood gene biomarker panels were discovered by microarrays and subsequently validated and cross-validated by qPCR. A total of 112 human PB samples, each paired with a graft biopsy, were analyzed (58 AR, 42 stable, and 12 other causes of graft injury). The differentially expressed genes by microarray, Q-PCR analysis of a four gene-set (GRB10, LGALS3BP, OLR1, and RNASE2) classified AR.

Results: We developed AR prediction model with the blood mRNAs by a binary logistic regression, and the AUC of the model was 0.76 in the training set. In addition, the decision curve analysis indicated a range of reasonable threshold probabilities for biopsy.

Conclusions: Therefore, we suggest blood mRNA signature may serve as a non-invasive monitoring tool of AR for a clinical application and can assist with deciding whether to perform a biopsy in a recipient with a rise in creatinine and probably justifies a biopsy.

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