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A Peripheral Blood Transcriptome Analysis and Development of Classification Model for Predicting Antibody-Mediated Rejection versus Accommodation in ABO-incompatible Kidney Transplant Patients

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Objectives: The major obstacles to successful ABO blood group incompatible (ABOi) kidney transplantation (KT) is antibody-mediated rejection (AMR). This study aimed to investigate the transcriptional profiles through RNA sequencing (RNA-seq) and to develop a minimally invasive monitoring tool for discrimination between accommodation and acute AMR in ABOi KT.

Methods: Eighteen ABOi KT patients with accommodation (ABOiA) and 10 ABOi KT patients with biopsy-proven acute AMR (ABOiR) at post-transplant 10th-day were selected. Complete transcriptomes of their peripheral blood at the time of biopsy were analyzed through RNA-seq. Candidate genes were selected through bioinformatic analysis, validated with quantitative PCR, and used for developing a classification model for predicting accommodation in ABOi KT patients.

Results: The number of genes that were differentially expressed in ABOiA compared to ABOiR was total 1385 genes with false discovery rate (FDR) at < 0.05. Functional annotation and gene set enrichment analysis showed several immune-related and immunometabolic pathways. A 5-gene classification model including COX7A2L, CD69, CD14, CFD, and FoxJ3 was developed by logistic regression. The model was further validated in an independent cohort from other hospitals, and represented 75% sensitivity, 100% specificity, and 80% accuracy to discriminate between ABOiA and ABOiR.

Conclusions: Our study suggests that the classification model based on peripheral blood transcriptomics could provide a new opportunity for minimally invasive diagnosis of acute AMR versus accommodation and subsequent patient-tailored immunosuppression in ABOi KT patients.