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Validation study of operational tolerance signature in Korean kidney transplant recipients

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Objectives: Operational tolerance (OT), defined as maintaining stable graft function without immunosuppression, is an ideal goal for kidney transplant recipients (KTRs). Recent investigations have demonstrated the distinctive features of gene signatures as well as the distributions of circulating lymphocytes in these patients. Nonetheless, substantial heterogeneities exist across studies. This study was conducted to determine whether previously reported candidate gene biomarkers and the profiles of lymphocyte subsets of OT could be applied in Korean KTRs.

Methods: Peripheral blood samples were collected from 153 patients, including 7 operationally tolerant patients. Quantitative real-time PCR and flow cytometry were performed to evaluate gene expression and lymphocyte subsets, respectively.

Results: Patients with OT showed significantly higher levels of B cell-related gene signatures (IGKV1D-13 and IGKV4-1), while T cell-related genes (TOAG-1) and dendritic cell-related genes (BNC2, KLF6, and CYP1B1) were not differentially expressed across groups. Lymphocyte subset analyses also revealed a higher proportion of immature B cells in this group. In contrast, the distributions of other B cells, including mature B cells and memory B cells, showed no difference across diagnostic groups. An OT signature, generated by the integration of IGKV1D-13, IGKV4-1, and immature B cells, effectively discriminated patients with OT from those in other diagnostic groups. Finally, the OT signature was observed among 5.6% of patients who had stable graft function for more than 10 years while on immunosuppression.

Conclusions: We validated an association of B cells and their related signature with OT in Korean KTRs.