

Oral Communication Abstract

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Discovery of cellular and genetic signatures of immune tolerance in kidney transplant recipients through single cell RNA sequencing analysis

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Objectives: Immune tolerance, defined by maintaining stable allograft function without immunosuppression after transplantation, is the ultimate goal of kidney transplant. Unlike bulk transcriptional analysis, single cell RNA sequencing (scRNA-seq) allows us to profile gene expression at the heterogeneous individual cell level. We aimed to investigate the difference of cellular and genetic signatures of immune tolerance in kidney transplant recipients (KTRs) through scRNA-seq analysis.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from 13 KTRs with immune tolerance (Tolerance, n=5), biopsy-proven allograft rejection (Rejection, n=4), and stable allograft function on maintenance immunosuppression (Stable, n=4) at 4 different transplantation centers. We used 20 cell surface marker antibody sequencing to cluster cell subsets, and 399 immune response panel to identify genetic expression difference at a single cell level. Single-cell distribution was visualized on UMAP plot.

Results: We generated 16,784, 10,180 and 7,280 single-cell transcriptomes of PBMCs from Tolerance, Rejection, and Stable groups, respectively. Ten known PBMC subsets were identified using cell surface marker antibody. Heatmap hierarchical clustering showed distinct differential cell surface marker expression in Tolerance group in comparison with other groups. The fractions of B cells and regulatory T cells in peripheral blood were increased in Tolerance group. B cell subsets showed that *Ybx3* (*Y-BOX binding protein 3*) was downregulated in Tolerance group, compared with Rejection (fold change 0.12) and Stable group (fold change 0.30). *S100A9* (*S100 calcium binding protein A9*) was highly expressed in Regulatory T cell subset of Tolerance group, compared with Rejection group (fold change 0.05).

Conclusions: It is the first study to identify difference in cellular distribution and genetic expression of immune tolerance in KTRs at single-cell resolution so far. Taken together with further scRNA-seq analysis of immune tolerance, it would provide us a better understanding of the mechanism and offer biomarkers to develop immune monitoring strategy, and allow cessation of immunosuppression.

Figure 1. Heatmap hierarchical clustering of cell surface marker

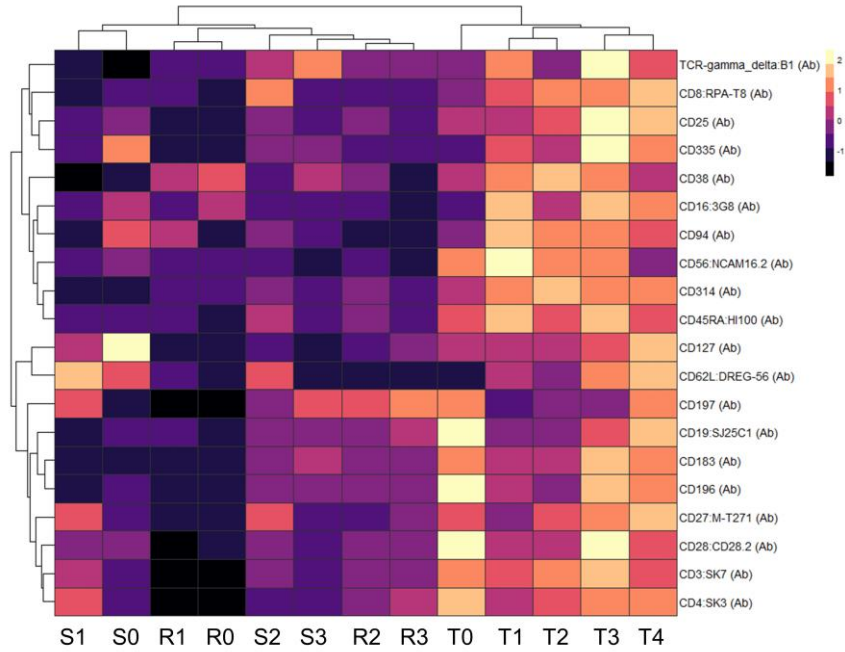


Figure 2. UMAP plot of single cells from PBMCs

