THE KOREAN SOCIETY OF NEPHROLOGY
APCN & KSN 2024
June 13(Thu) - 16(Sun), 2024 Coex, Seoul, Korea
Promoting Sustainable Kidney Health:
The Asia-Pacific and Beyond

Abstract Submission No.: A-0438

Single-nucleus RNA-seq reveals cell-type specific molecular signatures and links to genome-wide risk variants of IgA nephropathy

Jeong Min Cho, Sehoon Park, Dong Ki Kim
Department of Internal Medicine-Nephrology, Seoul National University Hospital, Korea, Republic of

Objectives : Single-nucleus RNA-seq (SnRNA-seq) is a valuable method for identifying cell-specific transcriptomic alterations in kidney cells. Our objective was to investigate SnRNA-seq data from biopsy-confirmed IgA nephropathy (IgAN) cases and identify cell-specific alterations in the transcriptome.

Methods : We collected snap-frozen kidney biopsy tissues from 6 cases of IgA nephropathy (IgAN) and 7 nephrectomy control cases. The disease control group included 3 cases of diabetic kidney disease, 6 cases of minimal change disease, and 6 PLA2R-Ab positive membranous nephropathy cases. SnRNA-seq was performed on the kidney tissues, and kidney cells were identified in the dataset through UMAP clustering. We investigated differences in the proportion of kidney cell types and identified differentially expressed genes (DEGs). Additionally, we searched for representative gene loci previously reported in a multiethnic genome-wide association study (GWAS).

Results : We successfully collected transcriptomic profiles of > 50,000 cells from IgAN, with a considerable enrichment of intraglomerular cells. The DEG analysis revealed a high number of DEGs in mesangial cells, fibroblasts, and vascular smooth muscle cells in the IgAN transcriptome compared to the nephrectomy and disease control cases. In the gene set enrichment analysis, the epithelial-mesenchymal transition pathway was enriched in the glomerular cells of IgAN. Furthermore, among various GWAS loci, ETS1 was the gene significantly highly expressed in the mesangial cells of IgAN, consistent across the compared control groups.

Conclusions : This investigation represents the largest SnRNA-Seq profiling of IgAN kidney cells to date. We identified notable enriched cell-specific pathways in IgAN. ETS1 may be a kidney-indwelling causal factor for IgAN pathophysiology, considering its notable significance in both previous GWAS results and the current SnRNA-Seq data.

Fig1.Study_flowchart.png

Figure 1. Overview of snRNA-seq of kidney tissues in glomerular diseases

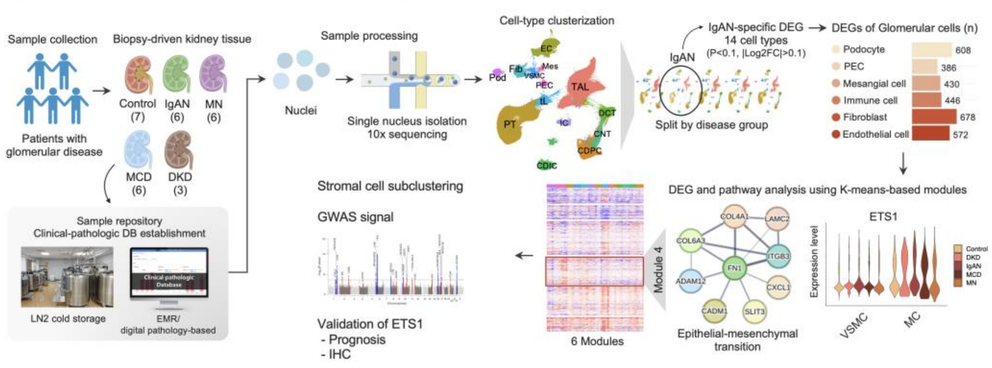

Fig1.Study_flowchart.png

Figure 2. Cell clustering and subtype proportion according to glomerular disease