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# Identification of Glomerulonephritis-Associated Differentially Expressed Genes by Spatial Transcriptomic Analysis

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**Objectives:** Glomerulonephritis (GN) encompass a group of immune-mediated kidney diseases which may share common gene expression pathways. We aimed to analyze the kidney substructure-specific gene expression profiles across various GN compared to the controls.

**Methods:** We performed spatial transcriptomic profiling using formalin-fixed paraffin embedded kidney biopsy specimens obtained from the controls and the patients with five types of GN (minimal change disease, membranous nephropathy, diabetic nephropathy, IgA nephropathy, and focal sclerotic glomerulosclerosis) using GeoMx Digital Spatial Profiler. Then, we compared the gene expression levels between each type of GN and controls in both glomeruli and tubules, and genes with false-discovery rate limits of 0.25 were considered as differentially expressed genes (DEGs). Using ToppGene suite, we detected functional enrichment of the DEGs based on gene ontology (GO) annotation.

**Results:** A total of 35 DEGs were found to be consistently downregulated in glomeruli across the five types of GN compared to control, whereas none of the DEGs were consistently upregulated. Twelve of 35 down-regulated DEGs, including two hub genes of FOS and JUN, were annotated with a molecular function GO term related to DNA-binding transcription factor activity and sequence-specific DNA binding. The annotated biological process GO term included response to lipid-related (17/35 DEGs), response to steroid hormone (12/35 DEGs), and positive regulation of DNA-templated transcription (12/35 DEGs) or cell cycle regulation (10/35 DEGs) GO terms. For cellular component GO terms, twelve of 35 DEGs were annotated with chromatin GO term. Regarding the highly expressed DEGs in the GN cases or DEG analysis with the tubule gene expression profiles, the spatial transcriptomic analysis results were diverse and a consistent DEG with the same directional change was not identified.

**Conclusions:** The glomerular GN gene expressions showed commonly downregulated DEGs related to cell cycling or transcriptional pathways, providing a clue for detecting therapeutic targets.