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Spatially resolved transcriptomic signature of relapsing minimal change disease

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Objectives: Minimal change disease (MCD) is usually responsive to corticosteroid. However, there are few data regarding the frequently relapsing MCD even after complete remission with previous treatment including corticosteroid. We aimed to investigate the molecular mechanisms of relapsing MCD using spatial transcriptomics.

Methods: We performed spatial transcriptomic profiling using GeoMx Digital Spatial Profiler with formalin-fixed paraffin embedded kidney biopsy specimens from four patients with relapsing MCD and various disease controls (MCD without relapse, focal segmental glomerulosclerosis, membranous nephropathy, diabetic nephropathy, and healthy controls). We compared the gene expression levels of relapsing MCD with the various disease controls in both glomeruli and tubules by DeSeq2 method. Differentially expressed genes (DEGs) were identified, and gene ontology (GO) term annotation and pathway analysis were performed.

Results: A total of 320 DEGs were consistently down-regulated in the glomerulus of relapsing MCD compared to all other various disease controls. Among the 320 DEGs, there are previously known genes that related to the pathogenesis of podocyte disease including NPHS1, NPHS2, and PODXL. GO annotation including cell adhesion molecule binding (GO:0050839), protein-containing complex binding (GO:0044877), MHC class II protein complex binding (GO:0023026) were the most notable annotated domain in the glomerulus of relapsing MCD. On the other hand, no DEG showed significance in the tubules between relapsing MCD and other disease controls.

Conclusions: In this study, we discovered consistently down-regulated DEGs in relapsing MCD compared with the various disease controls through spatial transcriptomics.

Volcano plot showing genes differentially expressed in relapsing MCD compared with A) MCD without relapse, B) healthy control, C) focal segmental glomerulosclerosis, D) membranous nephropathy, and E) diabetic nephropathy from glomerulus