외국 연수회원 발표

신사구체 질환의 transcriptome

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Molecular Mechanism of Glomerular Filtration Barrier Failure: Defining a Shared Transcriptional Response in Human Nephrotic Glomeruli

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Nephrotic syndrome is defined by morphological and functional alterations of glomerular filtration barrier (GFB). We hypothesized that a common pathogenic processes is activated in GFB failure. To test this hypothesis, we used genome-widegene expression profiling of glomeruli isolated from three types of nephrotic syndrome with primary involvement of podocytes; focal segmental glomerular sclerosis (FSGS, n=13), membranous glomerulopathy (MGN, n=21), and minimal change disease (MCD, n=6). Forty Affymetrix HGU133A based expression levels were analyzed using a customized data processing pipeline (www.GenePattern.org) and compared with 20 pre-transplant living donor kidney tissues as control.

In FSGS, 2025 probe sets were significantly ($p<0.01$) regulated, 3378 in MGN, and 2926 in MCD. Molecular signatures segregated nephrotic glomeruli from controls. Among the significantly regulated gene probe sets, 302 probes were commonly regulated in all three disease groups, of which 54 genes were also enriched in glomeruli compared to tubular compartments, including the newly-discovered familial nephrotic syndrome gene PLCE1. These genes were involved in biological functions of post-transcriptional modification, immune response, cell-to-cell and intracellular signaling, cell adhesion, actin cytoskeleton organization and biogenesis, cellular growth and proliferation. Canonical pathways annotated to the genes were cAMP, G-protein α, calcium dependent NF-AT, actin cytoskeleton, PDGF, and angiotensin signaling. De novo gene network mapping suggested that TNF, interferon and retinoic acid associated genes were key nodes in the common gene set.

Glomeruli-specific genome-wide gene expression profiling of three different types of nephrotic syndrome identified a common molecular fingerprint in nephrotic syndrome. Further investigation of the underlying transcriptional control processes can be used to define promising treatment targets in nephrotic syndrome.