특별강연 II

Proteinuric Kidney Diseases : Genes and Mechanisms

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A wide spectrum of immune mediated, infectious and genetic kidney and systemic diseases can present with nephrotic syndrome. Nephrotic syndrome reflects abnormalities in the glomerular filtration barrier and podocyte injury and dysfunction is the common thread. Recent genetic studies identified the podocyte-enriched proteins nephrin, podocin, PLCE, α-actinin-4 and TRPC6 as target genes of familial forms of nephrotic syndrome and FSGS. Podocytes are important for glomerular biology and pathology because they line the outer aspect of the GBM and form the final barrier to protein loss. Podocytes are highly differentiated cells with limited capability to undergo cell division in the adult and loss of podocytes is a hallmark of progressive renal disease. Podocytes display a complex cellular architecture consisting of cell body, major processes, and foot processes (FP). The FP form a characteristic interdigitating pattern with FP of neighboring podocytes leaving in between the filtration slits that are covered by the slit diaphragm. Functionally, the FP are defined by three membrane domains: i) the apical membrane domain, ii) the SD protein complex, and iii) the basal membrane domain or sole plate. All three FP membrane domains are linked to the highly dynamic FP actin cytoskeleton. Here we will review how proteins that regulate the plasticity of the podocyte actin cytoskeleton contribute to the maintenance of the glomerular filtration barrier. In particular we will focus on recently identified novel anti-proteinuric signaling pathway and the emerging concept that the onset of podocyte FP effacement and proteinuria represents a migratory event.