특별강연 II'

Molecular Insight into the Anti-proteinuric Action of Cyclosporine A

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Cyclosporine A (CsA) is the immunosuppressor most frequently used in transplant surgery. CsA binds to cyclophilins and the resulting complex inhibits the protein phosphatase calcineurin, thereby preventing the activation of T-cells. It is well known that CsA can induce a remission of proteinuria caused by human diseases ranging from MCD and FSGS to MN. The salutary action of CsA on proteinuria was generally attributed to the CsA mediated inhibition of NFAT signaling in T-cells. We have recently showed that LPS induced proteinuria, mimicking MCD, occurs independent of T- and B-lymphocytes. We also found that mice lacking synaptopodin, a key regulator of the podocyte actin cytoskeleton, display impaired recovery from LPS induced proteinuria. Finally, several studies have shown that CsA also reduces proteinuria in human and experimental Alports syndrome, a non-immunological disease, thereby raising raises doubt about the hypothesis that the anti-proteinuric effect of CsA results from its immunosuppressive activity. Here we discuss novel findings showing that the podocyte is a novel direct target of the anti-proteinuric action of CsA.