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당뇨병성 신손상에서 MYH9의 역할

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MYH9 as a New Culprit in Diabetic Kidney Injury

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Aim: The myosin heavy chain gene nine (MYH9) is a podocyte-expressed gene encoding a nonmuscle myosin IIA heavy chain. MYH9 is a cytoskeletal contractile protein that plays a role in several important cellular functions, including cytokinesis, cell motility and maintenance of cell shape. Though single nucleotide polymorphisms (SNPs) in the MYH9 gene have been reported to explain most of the excess risk of nondiabetic chronic kidney disease (CKD) in African-Americans, some studies have also shown association with diabetic end-stage renal disease (ESRD). But the disease causal mechanisms responsible for these MYH9-related glomerular diseases are not understood. Here, we investigated the association of MYH9 in type 2 diabetes mellitus (T2DM)-associated kidney injury and its role on podocyte biological function.

Methods: In vivo studies were done on type 2 diabetic db/db mice and Otsuka Long-Evans Tokushima Fatty (OLETF) rats. Conditionally immortalized murine podocytes or MYH9-siRNA-transfected podocytes were treated with angiotensin II (Ang II), a key mediator of diabetic kidney injury for 72h. Podocyte migration, adhesion, and permeability were assessed. Gene and protein expression were examined by real-time RT-PCR, Western blot and immunofluorescence.

Results: Renal MYH9 expression was decreased at RNA and protein levels in T2DM with markedly increased albuminuria. MYH9 expression by podocytes was increased during their in vitro differentiation. Ang II stimulation induced decreased expression of MYH9, as well as nephrin in podocytes. Ang II and MYH9 silencing caused reorganization of actin cytoskeleton, increased cell migration and albumin permeability of a podocyte monolayer, and reduced cell adhesion. Further study revealed that expression of adhesion-related molecules, α-actinin-4 and integrin β1 was lowered.

Conclusion: These results suggest that MYH9 interacts with integrin β1 through F-actin and α-actinin-4 and strengths the podocyte-GBM interaction thereby stabilizing glomerular architecture and preventing albuminuria in diabetes.
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