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Glomerular disease

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The role of MYH9 in diabetic kidney injury

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Background: MYH9 is a podocyte-expressed gene encoding a nonmuscle myosin IIA heavy chain and plays a role in several important cellular functions. Despite several groups have investigated extensively to understand the role and function of MYH9 in glomerular disease using animal models, little is known. Here, we investigate the relevance of MYH9 in diabetic-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. In vitro, we knocked down MYH9 gene by target siRNA in podocytes. MYH9 siRNA-transfected podocytes were treated with angiotensin II (Ang II), a key mediator of various kidney injury, for 72h. Podocyte cytoskeleton, migration, adhesion, and permeability were assessed. Gene and protein expression were examined by real-time RT-PCR, western blot and immunofluorescence.

Results: MYH9 expression was decreased at RNA and protein levels on podocytes of glomeruli in diabetic nephropathy. Ang II stimulation induced decreased expression of MYH9, as well as synaptopodin and nephrin in differentiated podocytes. Knockdown of MYH9 resulted in morphological changes by reorganization of actin cytoskeleton, reduced cell adhesion, and increased cell migration and albumin leakage than cells expressing MYH9. MYH9 deleted-podocytes were more susceptible to induce those defects under Ang II stimulation. Downregulation of MYH9 expression increased reactive oxygen species(ROS) level of podocytes with the induction of Nox4 and ROS blocking attenuated MYH9 depletion-induced disruption of podocyte actin cytoskeleton and albumin permeability.

Conclusion: These results suggest that MYH9 is a key component to maintain the biological function of podocytes. Loss of MYH9 is spontaneously involved in the progression of podocyte dysfunction induced by ROS and is more susceptible to progress podocyte defects under diabetic conditions.

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