Patients with poorly-controlled diabetes mellitus sustain damage to the macro and microvasculature that is responsible for much of the morbidity and mortality associated with the disease. In the kidney, dysregulation of glomerular blood flow has been implicated as one factor in the pathogenesis of diabetic glomerulosclerosis. Increased expression of adaptor protein p66Shc has been associated with progression of diabetic nephropathy. Afferent arteriolar dilation and glomerular hyperfiltration in diabetes are due to increased KATP channel availability and activity. Hyperglycemia was induced in Dahl SS (SS) rats in a model of type 1 diabetes via injection of streptozotocin (STZ). Albuminuria and glomerular injury were evaluated in SS and genetically modified SS lacking either p66Shc (p66ShcKO) or expressing p66Shc mutant (p66Shc-S36A). Afferent arteriolar diameter responses during STZ-induced hyperfiltration were determined using the juxtamedullary nephron technique to assess the role of p66Shc in KATP activity. Albuminuria and glomerular injury were mitigated in p66ShcKO and p66Shc-S36A rats with STZ-induced diabetes. SS rats with STZ-induced diabetes had a significant increase in the afferent arteriolar diameter, whereas p66ShcKO and p66Shc-S36A rats did not. STZ SS rats, but not STZ p66ShcKO or p66Shc-S36A rats had an increased vasodilator response to KATP channel activator pinacidil. Likewise, KATP inhibitor glibenclamide resulted in a greater decrease in afferent arteriolar diameter in STZ SS rats compared to STZ-treated SS p66ShcKO and p66Shc-S36A rats. Taken together, these results indicate that deletion of the adaptor protein p66Shc decreases afferent arteriolar KATP channel activity and decreases renal damage in diabetic SS rats.

Biography

Andrey Sorokin graduated from the St Petersburg State University and received his PhD from the Institute of Cytology Academy of Sciences of Russia in 1981. He is a Head of the Laboratory at the Medical College of Wisconsin, where he is holding the position of Full Professor with secondary appointments at Department of Physiology and Department of Microbiology & Immunology. He has published more than 100 papers in reputed journals and serving as an editorial board member of a number of journals including Frontiers in Renal and Epithelial Physiology.

p66Shc regulates vascular dysfunction and renal damage in diabetic nephropathy

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