Diabetic Chronic Kidney Disease
-Pathogenesis and Factors of Progression-

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Diabetic nephropathy (DN) is the leading cause of end-stage renal disease in the developed countries including Korea. In 2016, prevalence of diabetes in Korea amounted to 13.7% of adults aged 30 and above. To our astonishment, no more than 48.1% of them were within the optimally controlled glycemia range of HbA1c < 7%. If the current situation continues, chronic complication of diabetes could bring about disastrous consequences to Koreans with diabetes in the near future.

DN, one of the chronic diabetes vascular complications, is characterized by proteinuria, elevated serum creatinine level, hypertension, and decreased eGFR. Hemodynamic and metabolic factors encompassing chronic hyperglycemia (glucotoxicity) and dyslipidemia (lipotoxicity) are considered two major culprits that help develop and progress DN, especially in type 2 diabetes. In hemodynamic aspect, glomerular hypertension with or without systemic hypertension which results from a net increase in single-nephron GFR owing to hyper-reabsoption of salt and glucose in the proximal tubule followed by tubuloglomerular feedback, concomitant with the afferent-arteriolar dilation and efferent-arteriolar constriction of glomerulus further deteriorates renal function in the early stage of DN. Moreover, chronic hyperglycemia renders an additive impact on renal injury through well-established pathologic molecular pathways; It is the production of advanced glycation end products, by products of polyol and hoxoamine pathways as well as the activation of protein kinase C that stimulate oxidative stress, inflammation and fibrosis in the kidney. According to the latest accumulating data, there are various factors that contribute to the progression of DN including repetitive episode of acute kidney injury, comorbid renal disease, vascular disease, high uric acid levels, systemic and local inflammation, and severe hyperglycemias. Of those factors, the prolonged and severe acute kidney injury is most critical in the progression of DN.

Based on the results of large scale randomized controlled trials, intensive glucose and blood pressure control, and rennin-angiotensin-aldosterone system blockade constitute the backbone of DN treatment. However, as these conventional treatments do not completely prevent or halt DN, it is urgently needed to seek for novel agents. In searching for novel therapeutic modalities, current research is focusing on investigating the intracellular signaling of anti-inflammatory, antifibrotic, and metabolic pathways. Some of the promising

therapeutic agents recently developed include incretins, sodium-glucose cotransporter 2 inhibitors, and AMP-activated protein kinase activators which are expected to confer promising effects with respect to renal as well as systemic perspectives in diabetic milieu.