특별강연 II

Abnormal Oxygen Metabolism in the Kidney: Final Common Pathway of CKD

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Recent studies emphasize the role of chronic hypoxia in the tubulointerstitium as a final common pathway to end-stage renal failure. In order to protect the kidney against various kinds of diseases including diabetic nephropathy, chronic glomerulonephritis, and hypertensive nephrosclerosis, understanding of chronic hypoxia in the tubulointerstitium as a final common pathway to end-stage renal disease is essential.

Angiotensin II plays acrucial role in hypoxia of the kidney. Angiotensin II damages the vasculature and induces fibrosis. Angiotensin II predominantly constricts efferent arterioles and decreases blood flow in post-glomerular peritubular capillaries. In addition, angiontesin II induces oxidative stress via activation of NADPH oxidase with subsequent alteration of oxygen metabolism and hypoxia. Thus, amelioration of hypoxia in the kidney is one of the important mechanisms of renoprotection by the renin-angiotensin inhibitors.

Oxidative stress is induced by imbalance of oxygen metabolism homeostasis, including hypoxia. As described above, oxidative stressper se changes oxygen metabolism and leads to a vicious cycle of hypoxia and oxidative stress. Our recent studies utilizing proteomics and microarray analysis revealed changes of expression of oxidative stress-related molecules in intimate association with hypoxia in the kidney.

Cells are endowed with a system against hypoxia, which is composed of hypoxia-inducible factor, HIF, and hypoxia-responsive element, HRE. Activation of the HIF/HRE system is sub-optimal in kidney diseases due to oxidative stress. Thus, HIF transcription factor at the center of many cellular hypoxic responses will be an attractive target for therapeutic manipulationin the future.

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