신장의 집합관에서 미토콘드리아의 역할

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The Role of Mitochondria in Collecting Duct in Mice

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Introduction: Mitochondria play a central role in generation of energy and regulation of reactive oxygen species. In various renal injuries including toxins, drugs, and ischemia, mitochondrial injury plays important role in renal injury. There are few model of mitochondrial injury in kidney. Also, there is few study for roles of mitochondria on collecting ducts. We generated collecting duct specific mitochondrial injury model. And, we evaluated the effects of mitochondrial dysfunction on collecting ducts.

Methods: For generation of collecting duct specific mitochondrial injury mice, CRIF flox/flox mice were bred with Hoxb7-Cre mice. We evaluated light microscopy, electron microscopy, the chemistries in blood and urine, and ion channels including AE1, VATPase, and Rhcg. For evaluation of influence of CRIF1 deletion on mitochondrial function, we measured O2 consumption and membrane potential in control and silencing RNA treated mIMCD cells. For evaluation of effect on UUO induced renal injury, We divided mice into the following 4 groups: CRIF1flox/flox (WT) group; CRIF1 flox/flox-Hob7 Cre (CRIF1-KO) group; WT UUO group; and CRIF1-KO UUO group. We evaluated inflammatory marker including MCP-1, osteopontin, and F4/80, and fibrosis marker including TGF-b, a-SMA. I measured 8-OHDG for oxidative stress.

Results: Inhibition of Crif1 mRNA in mIMCD cell reduced O2 consumption and membrane potential. There are no significant differences in blood and urine chemistry including Na, K, Cl, urea nitrogen, and creatinine between WT and CRIF1-KO mice. Urinary pH was reduced in CRIF1-KO mice compared with WT mice. However, there are no significant differences of arterial blood pH and ion channel (AE1, VATPase, Rhcg expressions of collecting duct between WT and CRIF1-KO mice. Renal expression of MCP-1, OPN, Numbers of F4/80 positive cells, TGF-b, a-SMA, and Masson Trichrome stained area were significantly increased in CRIF1-KO-UUO kidneys compared with WT UUO kidneys., Urinary 8-OHDG was increased in CRIF1-KO-mice compared with WT mice. Also, Crif1-KO mice showed significantly increase of 8-OHDG-positive cell recruitment compared to WT mice. CRIF1-KO-UUO-kidneys were shown more increase recruitment of 8-OHDG-positive cells compared to WT-UUO-kidneys.

Conclusion: Collecting duct specific mitochondrial injury induced acidic urine and increase of oxidative stress. Oxidative stress induced by mitochondrial injury aggravates UUO induced renal injury.

Key Words: 일측요관폐쇄, 미토콘드리아, 집합관
UUO, Mitochondria, Collecting duct