심포지엄 X

Mitochondria in Renal Diseases: Animal Models of Kidney-specific Mitochondrial Dysfunction

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Mitochondria are cytoplasmic organelles in eukaryotic cells that performs distinct vital functions, including energy generation (oxidative phosphorylation), metabolism and integration of signaling for apoptosis. Impaired oxidative phosphorylation, the common final pathway of mitochondrial metabolism, results in a variety of clinical manifestations, and in the other hand, acute and chronic diseases processes affect these mitochondrial functions.

Kidney accomplishes various important physiological processes through the coordinated actions of differentiated cells including glomerular endothelial cells, podocytes, tubular cells and other ductal cells. The mitochondrial in these specialized cells are believed to be involved in the disease processes of kidney disease. Unfortunately, the lack of animal models which show the cell-type specific mitochondrial dysfunctions in kidney limits our understanding of mitochondrial roles in the progression of kidney diseases.

We isolated a mitochondrial protein, called mtCRIF1, which is localized in mitochondria. In the subsequent studies, we found that mtCRIF1-deficient cells showed marked deterioration of mitochondrial function resulted from loss of assembly in oxidative phosphorylation (OXPHOS) I, III and IV complexes. In addition, we show that human or mouse cells lacking exhibit markedly destabilized supercomplexes. CRIF1-deficient cells shows high lactate production and enhanced dependency on glycolytic ATP generation, due to severe reduction of respiratory chain complex activity. Although CRIF1 itself seems not a part of oxphos complex, CRIF1-deficient cells exhibit a reduced contents of complex I, III, IV and of its components, suggesting that CRIF1 plays key roles in the mitochondrial biogenesis and/or the maintenance of mitochondrial oxphos supercomplex.

We have developed the mice models which showed mitochondrial dysfunctions by gene targeting in the specific cell types, e.g., collecting duct and podocytes in kidney. In this symposium, the phenotypes of those model mice are going to be discussed. In summary, mitochondrial CRIF1 (mtCRIF1) is essential for the maintenance of normal mitochondrial oxphos functions and its dysregulation may be possibly linked to kidney disorders related to cellular energy metabolism.