특별강연

# Mitochondrial Biogenesis and Its Implications in Metabolic and Renal Diseases

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Mitochondrial ribosomes (mitoribosomes) decode the genetic information supplied by mtDNA to synthesize 13 OXPHOS proteins at the inner mitochondrial membrane. Mitoribosomes have a higher protein content than the ribosomes involved in other translation systems, suggesting that mitoribosome-specific proteins have replaced RNA structural elements during evolution. Despite having a lower RNA content, the mammalian mitoribosome is physically larger than the bacterial ribosomes because of the new proteins added throughout evolution. The identification of these additional proteins in mammalian mitori- bosomes is critical to understand the regulation of the OXPHOS system in mammals.

We have characterized a mitochondrial factor, CRIF1, which is essential for intramitochondrial production and the subsequent insertion of OXPHOS polypeptides into the inner mitochondrial membrane. CRIF1 interacts with LSU proteins, some of which surround the exit tunnel of the mitoribosome, and also interacts with nascent OXPHOS polypeptides and the mitochondrial-specific chaperone Tid1. The essential role of CRIF1 in mitochondrial synthesis and membrane integration of OXPHOS polypeptides was shown in brain-specific *Crif1*-deficient mice, which exhibited profound OXPHOS failure and marked neurodegeneration. Type 2 diabetes is one of the most challenging health problems in the 21st century. Although insulin resistance is regarded as a fundamental defect that precedes the development of type 2 diabetes, the nature and cause of insulin resistance remain unknown. To determine whether adipose deficiency of mitochondrial respiratory capacity plays an etiological role in systemic insulin resistance, the metabolic phenotype of mice with mitochondrial OXPHOS (oxidative phosphoryla- tion)-deficient adipose tissue was examined. Crif1 is a protein required for the translation of mtDNA-encoded OXPHOS subunits. Interestingly, mice haploinsufficient for Crif1 in adipose tissue showed reduced OXPHOS capacity and developed marked insulin resistance. In this symposium, etiological roles of mitochondrial dysfunction caused by organ-specific Crif1 deficiency in metabolic and renal diseases will be discussed.

## References

1) Ryu MJ et al. Crif1 deficiency reduces adipose OXPHOS capacity and triggers inflammation and insulin resistance in mice. PLoS Genet. 2013
2) Ryu MJ et al. Mitochondrial oxidative phosphorylation reserve is required for hormone- and PPARγ agonist-induced adipogenesis. Mol Cells. 2013
3) Kim SJ et al. CRIF1 is essential for the synthesis and insertion of oxidative phosphorylation polypeptides in the mammalian mitochondrial membrane. Cell Metab. 2012