Effect of *Monascus Purpureus* Rice on Electronegative LDL-Induced Mitochondrial Dysfunction in Cardiomyocytes

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BACKGROUND: Dyslipidemia, especially high levels of low-density lipoprotein cholesterol (LDL-C) or increasing of triglycerides (TGs), is recognized as an important risk factor for cardiovascular diseases (CVDs). Growing studies have shown that the electronegative low-density lipoprotein (L5) is the real atherogenic factor in dyslipidemia, which leads to CVDs. In addition to the inflammatory and apoptotic effects in endothelial cells, our previous studies have found that L5 could also induce cardiac dysfunction. *Monascus purpureus* rice have been claimed to improve blood circulation by decreasing cholesterol and triglyceride levels in both human and mice. Our previous study has found that *M. purpureus* rice could reduce plasma L5 level and diminish L5-induced cardiac dysfunction. However, the underlying mechanisms are still not completely clear.

MATERIALS AND METHODS: Syrian hamsters (8 weeks) were fed with normal diet, high fat diet (HFD) or HFD and *M. purpureus* rice (20 mg/kg/day) for 3 months and the percentage of plasma L5 was analyzed by fast performance liquid chromatography. Effect of L5 on energy production of mitochondria was assayed by Seahorse XF-24 extracellular flux analyzer. Mitochondrial swelling assay were also used to determine its function in isolated mitochondria. Interaction between L5-associated lipoproteins and mitochondria was examined by immunofluorescence in H9c2 cardiomyoblasts with Mitotracker Red FM and corresponding probes. Immunoprecipitation and western blot was used to determine the protein-protein interaction and protein expression levels.

RESULTS: L5-associated Apo E has been found to be internalized into H9c2 cardiomyoblast in 30 minutes and translocated to VDAC on mitochondria in 16 hours. The translocation of ApoE could induce dissociation of hexokinase-2 from VDAC, which may be the mechanism underlies mitochondria swelling and decreased maximal respiration of mitochondria. On the other hand, *M. Purpureus* Rice could significantly decrease plasma L5 level in hamsters with HFD with unknown mechanism.

CONCLUSION: In conclusion, we have shown that *M. purpureus* rice could reduce plasma L5 level in endogenous L5 animal model and prevent electronegative LDL L5-induced mitochondria fission and cardiac dysfunction by the mechanism of drp-1 and Apo E-mediated abnormal mitochondria energy production and swelling.