Calmodulin dependent protein kinase (CaMK)II activation by exercise regulates NRF-1 and its target lipid oxidizing target gene, *Cpt-1* in rat skeletal muscle

Regular exercise increases oxidation of fatty acids in skeletal muscle. Exercise activates Calmodulin-dependent protein kinase (CaMK)II, resulting in increased mitochondrial oxidative capacity. As such, exercise can curb accumulation of excess lipids in adipose and intramuscular tissues that may result in obesity/type 2 diabetes. Lipid metabolism mainly occurs in mitochondria regulated by NRF-1 and is controlled by a set of mitochondrial enzymes. For example, Carnitine palmitoyltransferase (CPT)-1 is a rate-limiting enzyme in mitochondrial lipid oxidation that regulates the transport of long chain fatty acids across the mitochondrial membrane, resulting in ATP synthesis. On the other hand, acetyl-CoA carboxylase (ACC)-1 is a mitochondrial enzyme that promotes lipid synthesis by providing malonyl CoA substrate for the biosynthesis of fatty acids. NRF-1 is the major transcriptional factor of the mitochondria, the site for ATP generation from carbohydrates and lipids. As such, mitochondrial dysfunction is crucial in metabolism of the cell. In order to investigate the amount of NRF-1 bound Cpt-1***, ChIP assay performed. Exercise showed that the amount of NRF-1 bound*** Cpt-1 ***was ~1.3 fold increase compared with the control group. e exercise + KN93 group did not show any signi cant change compared with the exercise group. is result indicates that exercise-induced CaMKII activation increase the amount of NRF-1 bound*** Cpt-1***. With respective to gene transcription, exercise group showed ~7.8 fold increase compared with the control group.*** Cpt-1 ***gene expression of the exercise + KN93 group showed signi cant decrease compared with the exercise group.*** Cpt-1 ***gene expression of the exercise + KN93 was similar to the control group. is result shows that CaMKII activation increase*** Cpt-1 ***gene expression in rat skeletal muscle. With respect to mitochondrial integrity, mitochondria size of the exercise group increased by ~3.0 fold compared with the control group, whereas the exercise + KN93 group showed signi cant decrease compared with the exercise group. Using TEM we show that exercise-induced CaMKII activation increases mitochondria size in rat skeletal muscle and its integrity.***

Biography

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