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CHRONIC EXERCISE REGULATES THE EXPRESSION OF MITOCHONDRIAL SIRTUINS IN MURINE SKELETAL MUSCLE

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Mitochondrial function in skeletal muscle plays a crucial role in the molecular mechanisms of ageing, sarcopenia, and insulin resistance. Therefore, maintenance of the mitochondrial integrity has been well-documented to be clinically important. In mammals, seven sirtuins (SIRT1-SIRT7) have been identified and display diverse functions and subcellular localizations. SIRT3, SIRT4 and SIRT5 are predominantly localized in mitochondria, and are thought to regulate mitochondrial functions and biogenesis via regulating post-translational modifications. Interestingly, chronic exercise increases Sirt3 expression, as well as mitochondrial biomass and activity, in skeletal muscle. Hence, it is likely that exercise regulates the expression of mitochondrial sirtuins, which, at least partly, induces mitochondrial adaptations. However, the physiological functions and exercise-induced responses of mitochondrial sirtuins remain unclear. Therefore, we investigated 1) whether the protein expression of mitochondrial sirtuins is correlated with mitochondrial proteins among metabolically heterogeneous murine skeletal muscles, 2) whether the chronic exercise increases SIRT3, SIRT4 and SIRT5 expression in murine skeletal muscle.

In order to evaluate the physiological functions of mitochondrial sirtuins in skeletal muscle, we investigated the relationship between the expressions of mitochondrial sirtuins and these of mitochondrial biogenesis-related proteins (PGC-1α, TFAM, and COX IV) among metabolically heterogeneous skeletal muscles. SIRT3 and SIRT5 similarly demonstrated significant correlations with mitochondrial proteins. By contrast, SIRT4 negatively correlated with mitochondrial proteins. We further examined whether chronic exercise regulates mitochondrial sirtuins expressions in skeletal muscles. Chronic running exercise significantly increased the protein expression of SIRT3 and SIRT5. On the other hand, the expression of SIRT4 was significantly decreased in runners.

There results suggest that muscular expressions of mitochondrial sirtuins are highly responsive to exercise and might regulate mitochondrial adaptations in physiological conditions. Therefore, SIRT3, SIRT4 and SIRT5 may mediate exercise-induced health promoting effects.

Keywords: mitochondria, sirtuin, exercise