Gga-let-7f-3p promotes apoptosis in selenium deficiency-induced skeletal muscle by targeting selenoprotein K.

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Abstract
Selenoprotein K (SELENOK) is primarily observed in the endoplasmic reticulum, and serves to maintain the normal physiological functions of skeletal muscle. Skeletal muscle development and regeneration are associated with significant changes in the expression of specific microRNAs (miRNAs). Downregulated SELENOK expression is observed in chicken muscles deficient of Se. However, the mechanisms of miRNA regulation of SELENOK expression remain elusive. Here, deep sequencing was used to detect the miRNA profiles of muscle in Se deficient (-Se group) and normal (C group) chickens. A dual-luciferase reporter assay was adopted to verify the relationship between SELENOK and gga-let-7f-3p. In addition, gga-let-7f-3p was either overexpressed or knocked-down in chicken myoblasts. Furthermore, the cells were treated with N-acetyl-l-cysteine (NAC) or hydrogen peroxide (H2O2) in order to probe the factors involved in oxidative stress, endoplasmic reticulum stress (ERS) and apoptosis, respectively. Relative to the C group, there were 132 differentially expressed miRNAs (including 57 upregulated and 75 downregulated) in the muscles of the -Se group. The dual-luciferase reporter assay showed that SELENOK was a primary target of gga-let-7f-3p. It was also observed that the overexpression or knock-down of gga-let-7f-3p significantly influenced the SELENOK expression. Moreover, NAC blocked mimics of ga-let-7f-3p, thus inducing oxidative stress, ERS and apoptosis. Simultaneously, gga-let-7f-3p inhibitors blocked the stimulant effects caused by H2O2 in chicken myoblasts. Furthermore, Se deficiency downregulated the SELENOK protein expression and induced oxidative stress, ERS and apoptosis in chicken muscles. In conclusion, the gga-let-7f-3p-SELENOK pathway played a pivotal role in Se deficiency mediated muscle injuries through the induction of oxidative stress and ERS, ultimately promoting apoptosis.