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CIRCULATING MIRNAS AS POTENTIAL BIOMARKERS FOR SKELETAL MUSCLE ATROPHY

**Abstract**

Muscle atrophy is a common physiological and pathological process, which occurs in response to fasting, chronic disease and disuse (e.g. long time bed rest and space flight). Muscle atrophy, induced by increased protein degradation and decreased protein synthesis, leads to the deterioration of disease and reduces the quality of life. Therefore, the diagnosis and treatment of skeletal muscle atrophy is an important clinical issue. So far, quantification of muscle weight is difficult. Many measurement methods were developed to detect skeletal muscle atrophy, including tomography, magnetic resonance imaging (M.R.I.), and dual-energy X-ray absorptiometry. These methods can detect muscle wasting but cannot indicate the possibility of developing muscle atrophy. Moreover, these methods are all expensive and only available at large institutions. Thus, it is necessary to discover new noninvasive biomarkers which are cheap and easily available for diagnosis in clinics. miRNAs are short noncoding RNAs that modulate gene expression on the post-transcriptional level and play key roles in a wide scope of physiological and pathological processes. However, there was no report about the correlation between serum miRNAs levels and disuse induced muscle atrophy. The main purpose of this study was to find potential circulating miRNA biomarkers for skeletal muscle atrophy diagnosis. Muscle biopsy has long been expected to be replaced by noninvasive biomarkers with diagnostic value and prognostic applications for muscle atrophy. Growing evidences suggest that circulating microRNAs could act as biomarkers for numerous pathophysiological statuses. In the present study, our results shown that the serum levels of six muscle-specific miRNAs (miR-1/23a/133/206/208b/499) were all elevated in unloading induced mice ( $P < 0.01$ ). And, the medium levels of these six muscle-specific miRNAs were all elevated in starvation induced atrophic C2C12 myotubes ( $P < 0.01$ ). Moreover, the serum levels of miR-23a/206/499 were induced in participants after 45 days of head-down bed rest (HDBR). And, the levels of miR-23a/206/499 were positively correlated with the ratio of soleus volume loss in HDBR participants, indicating that they might represent the process of muscle loss. In Conclusion, our results demonstrated that circulating miRNAs could serve as useful biochemical and molecular indicators for muscle atrophy diagnosis and disease progression.