(RNA Interference–Mediated Recovery of Skeletal Muscle Function for the Prevention of Frailty)

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In super-aged societies such as Japan, the prevention and management of frailty constitute pressing healthcare challenges. In our previous study, we demonstrated that inhibition of microRNA Let-7 upregulates Igf2bp2 expression, suppresses the expression of muscle atrophy-related genes, and enhances glucose uptake in myotubes. However, the effects of Let-7 inhibition on frailty prevention at the organismal level remain unclear. In the present study, we generated skeletal muscle-specific Let-7 knockout mice (Flox group) and evaluated their phenotype using a frailty model induced by high-fat diet loading. Compared with control mice, the Flox group exhibited significantly attenuated increases in body weight and visceral fat accumulation. However, no significant improvements were observed in skeletal muscle mass or grip strength, indicating a lack of direct anti-sarcopenic effects. These findings suggest that skeletal muscle-specific inhibition of Let-7 may contribute to frailty prevention primarily through the suppression of fat accumulation, rather than through direct effects on muscle preservation. This strategy may hold promise for future therapeutic applications targeting obesity-related frailty.