SIRT1, an NAD$^+$-dependent protein deacetylase, maintains oxidative muscle fiber in the skeletal muscle and contributes to exercise capacity in mice.

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[Background and Aim]

We previously reported that resveratrol, an activator of an NAD$^+$-dependent deacetylase SIRT1, improves exercise tolerance with upregulation oxidative type of muscle fibers in a mouse model of Duchenne muscular dystrophy. SIRT1 deacetylates and activates PGC-1α, a co-activator to promote expression of oxidative muscle fibers. Here, we examined whether SIRT1 maintains oxidative muscle fibers for exercise capacity in the skeletal muscle.

[Methods and Results]

We first compared the expression level of SIRT1 in several types of skeletal muscles in wild-type mouse (WT). The SIRT1 protein level was the highest in the soleus muscle (+3.5-fold), which is mainly made up of oxidative fibers, compared to the other glycolytic muscles such as quadriceps, gastrocnemius, tibial anterior, and extensor digitorum longus muscles. The SIRT1 mRNA level was most abundant also in the soleus muscle. Immunohistological analysis using soleus muscle sections showed that the percentage of type IIa, one of oxidative muscle fibers, was significantly lower in the skeletal muscle-specific SIRT1 knockout mouse (SIRT1MKO) than that in WT (42% vs. 56%) at 79-98 weeks of age. In contrast, the percentage of glycolytic type IIx+IIb fibers was higher in the SIRT1MKO (15%) compared to WT (11%). Treadmill running distance at 15 weeks of age was significantly shorter in SIRT1MKO (158 ±10 m) than that in WT (1088±33 m).

[Conclusion]

These results suggest that SIRT1 maintains exercise capacity by preserving oxidative muscle fibers in the skeletal muscle.