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2. Title
   Roles of FGF21 in the Relationship between Sarcopenia and Smoking

3. Period
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4. Summary
   FGF21, known as an endocrine factor, is one of the metabolic regulators and its level in blood is increased by high-fat diet and smoking. FGF21 is also known as an anti-inflammatory factor. Inflammation causes skeletal muscle atrophy, suggesting that FGF21 may work to maintain muscle mass. In this study, we attempted to elucidate the significance and mechanism of FGF21 in the changes in muscle mass and muscle strength induced by high-fat diet and treatment with nicotine, a major component of smoking, and also to develop a method to inhibit skeletal muscle atrophy via FGF21.

   We observed a significant decrease in muscle strength and muscle mass in FGF21 knockout mice fed on a high-fat diet when nicotine was administered. Degradation of skeletal muscles was enhanced in FGF21 knockout mice under the same conditions, and inflammatory changes in macrophages of secondary immune organs and increased blood levels of inflammatory cytokines were observed. The production of IL-6 by free fatty acids was enhanced by nicotine in cultured macrophages and decreased by FGF21 treatment. Considering the possibility that FGF21 can inhibit skeletal muscle atrophy by suppressing inflammation, oral administration of fenofibrate, which induces FGF21 in the liver, was shown to improve atrophy of the gastrocnemius muscle by nicotine and high-fat diet. On the other hand, the soleus muscle was reduced by fenofibrate. It will be necessary to develop methods that can inhibit lifestyle-induced atrophy in any type of skeletal muscle, by expanding on the findings of FGF21 signaling obtained in this study.