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2. Title

   Analysis of the Molecular Mechanism of Nicotine's Antiobesity Action with the Imaging of Skeletal Muscle Thermogenesis

3. Period

   2016-2017

4. Summary

Skeletal muscle thermogenesis has a large impact on energy expenditure of animals. It is generally known that cigarette smoking decreases body weight. Although nicotine is a sympathomimetic agent that increases resting energy expenditure, its direct effect on skeletal muscle energy consumption is unclear. To visualize thermogenesis of skeletal muscle at an organelle level, we introduced thermosensor GFP fused with endoplasmic reticulum-targeting sequence (tsGFP-ER) to the tibialis anterior (TA) and flexor digitorum brevis (FDB) muscles of C57BL/6 mice with an adeno-associated virus (AAV) vector. Fourteen to twenty days after viral infection, tsGFP-ER was expressed in most fibers in both TA and FDB muscles. Immunocytochemical analysis showed that tsGFP-ER was localized in the longitudinal sarcoplasmic reticulum of FDB fibers. An increasing temperature of perfusion solution changed the ratio of fluorescence excited with 405 to 488 nm light (405/488 ratio) in isolated FDB fibers expressing tsGFP-ER. An addition of sarcoplasmic-endoplasmic Ca^{2+} ATPase inhibiter also changed 405/488 ratio. These results suggested that tsGFP would be useful tool to examine the thermogenesis and energy expenditure of the skeletal muscle at an organelle level. However, since the sensitivity of this method may not enough to detect the thermogenesis *in vivo*, further improvement will be necessary.