Mitochondrial specific peptides as novel therapeutics against sarcopenia

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Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength by chronic diseases, aging, and lack of exercise for a long period of time. One of the common characters of the disease includes alterations in mitochondrial function. Mitochondrial dysfunction in skeletal muscle cells are mainly derived from an increase of reactive oxygen species (ROS) inside of the organelle, resulting in muscle loss and a decrease in exercise capacity. We have been developing mitochondria-specific peptides, which can reduce ROS generation, correcting mitochondrial dysfunction derived from ROS. In this study, we try to reverse muscle dysfunction by our mitochondrial specific peptides in two different pathogenic animal models for sarcopenia. One model is a Drosophila model with phosphatidylserine synthase (Pss) mutation, which generates phenotypes of muscular dystrophy mutation. The other model is an old female mouse, where mitochondria in skeletal muscle are severely damaged in shapes and numbers. Treatment of the mitochondrial specific peptide to the Pss-mutated Drosophila model resulted in enhanced locomotive capacity of larva-stage fly as well as proper development of flight muscle in adult-stage fly. Treatment of the peptide to old mouse also showed enhanced exercise capacity with correcting mitochondrial morphology. Furthermore, the drug has synergistic effect with common exercise therapy, doubling the exercise capacity relative to the sedimentary control mouse. The improved capacity is owing to increasing mitochondrial number and erasing abnormal mitochondrial morphology in skeletal muscle. Correctively, mitochondrial-targeted peptides, reversing the mitochondrial dysfunction and improving athletic ability of animals in two different models, may be to clinical trials for therapeutics against sarcopenia.