

Department of Molecular Physiology Division of Physical Fitness

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General Summary

Research activities in our division have been focused on the plasticity of skeletal muscle and preventive medicine against metabolic syndrome in terms of exercise physiology.

Research Activities

Ubiquitin proteasome and autophagy-lysosome systems in unloading induced skeletal muscle atrophy

Ubiquitin proteasome systems are considered to act in coordination with autophagy-lysosome systems. We investigated the involvement of neural precursor cell expressed developmentally down-regulated protein 4 (Nedd4) and autophagy-related proteins in unloading induced muscle atrophy with a specific focus on age dependency. Unloading induced higher expression of ubiquitin ligase Nedd4 and autophagy-related proteins, especially in aged rats, independently of intermitted reloading sufficient for preventing atrophy. Reloading may have induced an anabolic process that overwhelms the catabolic process of the ubiquitin-autophagy system.

Site-specific effects of nutrition and exercise on rat musculoskeletal system

Both nutrition and exercise are necessary to maintain musculoskeletal function. We studied the site-specific effects of nutrition and exercise on the musculoskeletal systems of growing rats. Dietary restriction suppressed exercise-induced down-regulation of myostatin with a corresponding increase in muscle mass in the plantaris muscle but not in the soleus muscle. Exercise selectively increased the bone volume and mineral density of trabecula in metaphyses. This increase was suppressed by dietary restriction. We concluded that dietary restriction suppresses the exercise-induced growth of the musculoskeletal system differentially in a site-specific manner.

Effects of daily exercise with dietary restriction on fatty liver and skeletal muscle morphology in Zucker fatty rats

Daily exercise and dietary restriction have been strategies for improving obesity-related diseases. We studied the effects of daily exercise or dietary restriction or both on fatty liver and the morphology of skeletal muscle in genetically obese Zucker rats. Daily exercise combined with dietary restriction, but not dietary restriction alone, improved insulin resistance, hyperlipidemia, fatty liver, and hepatic fatty acid oxidation with higher expression of carnitine palmitoyl-coenzyme A transferase 1. In addition, daily exercise combined with dietary restriction attenuated lipid accumulation and mitochondrial swelling within myofibers. These findings correlated with improvements in insulin resistance and

may reflect the amelioration of lipid metabolism.

Astaxanthin supplementation effects on adipocyte size and lipid profile in Otsuka Long Evans Tokushima Fatty rats

We investigated the effects of astaxanthin supplementation (2 g/kg diet powder chow food) on visceral adipose tissue and the lipid profile in Otsuka Long Evans Tokushima Fatty rats, an animal model of hyperphagia and visceral fat accumulation. Astaxanthin supplementation for 6 weeks promoted the size reduction of visceral adipocytes, decreased free fatty acid levels, and increased the serum level of high-density lipoprotein cholesterol. These results suggest that astaxanthin can at least partially ameliorate the obesity-related lipid profile and adipocyte abnormalities.

Clinical definition and diagnostic criteria for sarcopenia

The occurrence of sarcopenia and muscular dystrophy with aging has been attracting more attention. Many factors are reported to cause sarcopenia, such as the functional decline of a digestive organ occurring with aging and malnutrition due to a decrease in food intake. Other reported causes of sarcopenia are decreases in growth hormones and increases in cytokines. Meanwhile, the differentiation between sarcopenia and the atrophy of disused muscles is unclear and their clear differentiation will be important in future studies. Recently, the diagnostic criteria of sarcopenia have been defined according to a large-scale investigation. In the future, an easier method of diagnosing sarcopenia should be developed. Specific treatment strategies more closely correlated to the clinical condition of individual patients must be designed, because the causes of sarcopenia vary widely. We attempted to summarize the characteristics of the clinical condition, diagnosis, and treatment of sarcopenia.

Publications

Kimura M¹, Iida M¹, Yamauchi H, Suzuki M, Shibasaki T, Saito Y¹, Saito H¹ (¹Keio Univ).

Astaxanthin supplementation effects on adipocyte size and lipid profile in OLETF rats with hyperphagia and visceral fat accumulation. *J Funct Foods*. 2014; **11**: 114-20.

Reviews and Books

Udaka J, Fukuda N, Yamauchi H, Marumo K. Clinical definition and diagnostic criteria for sarcopenia. *Journal of Physical Fitness and Sports Medicine*. 2014; **3**: 347-52.