Pleiotropic Effects of Exercise and Food Factors on Life-style Related Diseases

Yuji Naito[1], Wataru Aoi[2], Tomohisa Takagi, and Toshikazu Yoshikawa[3]
[1]Molecular Gastroenterology and Hepatology, Kyoto Prefectural University of Medicine, Kyoto 602-866, Japan
[2]Laboratory of Health Science, Graduate School of Life and Environmental Sciences, Kyoto Prefectural University, Kyoto 606-8522, Japan

Recent studies have clearly implicated several lifestyle risk factors, including tabacco consumption, diet and obesity, to be associated with increased risk of colon cancer. Although physical inactivity is now recognized as a risk factor for several chronic diseases including cancer, only a very limited number of studies have evaluated the association between physical activity and colon carcinogenesis. The IARC concluded that the evidence supports a causal relation between inactivity and colon cancer risk (Eur J Cancer Prev 2002). We recently investigated the effects of reactive oxygen species (ROS) and antioxidants on lipid metabolism in skeletal muscle during exercise, because it is important for health promotion associated with the reduction of obesity to regulate the metabolism of carbohydrates and lipids. Exercise groups performed treadmill running exercise 2 days per week. By training, the weight of epididymal fat was significantly decreased, but gastrocnemius muscle weight was not changed. Coimmunoprecipitation of FAT/CD36 with CPT1 (carnitine parmitoyltransferase 1) in skeletal muscle showed a significant increase after exercise, indicating the increase of the interaction between CPT1 and FAT/CD36 as well as the promotion of lipid metabolism. The respiratory exchange ratio (RER) calculated by VO_2 and VCO_2 was decreased and fat utilization was increased in mice after exercise. These data clearly indicate that exercise promoted lipid metabolism via CPT1 activation. More interestingly, we found that CPT1 proteins were modified by hexanoyl-lysin (HEL), an active metabolite of lipid peroxides, after exercise, and that this oxidative modification was clearly reversed by the treatment with astaxanthin, an antioxidative carotenoid. Astaxanthin treatment also enhanced the CPT1 interaction with FAT/CD36 and the lipid metabolism, indicating that astaxanthin can modify muscle metabolism via its antioxidative effect, resulting in the improvement of muscle function in exercise. In addition to the effect of exercise on lipid metabolism, muscle cells after exercise may play a role in the colon carcinogenesis by the production of some proteins. In the next study, we investigated the effect of exercise on azoxymethane (AOM)-induced colon carcinogenesis in mice. By the analysis of proteomics approach, we determined a candidate protein, SPARC1 (secreted protein acidic and rich in cysteine 1), to play a role in the inhibition of AOM-induced tumorgenesis by exercise. SPARC1-deficiecy cancelled the inhibitory effect of exercise against colon tumorgenesis.

In conclusion, exercise plays an inhibitory role against colon cancer by the promotion of lipid metabolism and the induction of SPARC1 in muscle cells.