Editorial

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Exercise-induced myokines for cancer patients: 7th in a series of scientific evidence

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All of the previous editorials in this series have reported on the benefits of exercise in improving immune function. However, the target of exercise rehabilitation for immunity enhancement has been limited to cancer patients. Cancer, another name for a malignant tumor, is associated with adverse changes in metabolically important tissues, including myocytes, adipocytes, and hepatocytes. Those changes include insulin resistance, hyperlipidemia, impaired mitochondrial function, inflammation, cancer cachexia, sarcopenia, and diminished strength. On the other hand, exercise powerfully improves all of these conditions in healthy humans, suggesting that exercise could be a strategy to counter metabolic derangements (Raun et al., 2021).

A skeletal muscle, which acts as a secretory organ, stimulates the production, secretion, and expression of cytokines or myokines derived from muscle fiber peptides. Exercise-induced myokines influence crosstalk between different organs in an autocrine, endocrine, or paracrine fashion. Myokines are recently recognized as potential candidates for treating metabolic diseases through their ability to stimulate AMP-activated protein kinase signaling, increase glucose uptake, and improve lipolysis (So et al., 2014). The benefits of exercise are widely known for preventing harmful effects of proinflammatory adipocytokines through muscle-secreted proteins. Interleukin (IL)-6 was the first and most well-known exercise-induced myokine to be identified in the bloodstream in response to skeletal muscle contractions (Pedersen and Febbraio, 2012). It is a peptide that plays an anti-inflammatory role by inhibiting tumor necrosis factor-α and improves glucose uptake by stimulating AMP-activated protein kinase signaling (Kahn et al., 2005). In 2011, Pedersen reported that myokines provide beneficial metabolic effects during crosstalk between skeletal muscle and liver, as well as skeletal muscle and adipose tissue. In other words, myokines constitute an important area of research in metabolic diseases such as obesity, diabetes mellitus, and cancer. To date, the myokines that have been reported in academia include IL-15, brain-derived neurotrophic factor, leukemia inhibitory factor, irisin, fibroblast growth factor 21, and secreted protein acidic and rich in cysteine. In addition to these myokines, this editorial introduces IL-15.

The IL-15 is a member of the IL-2 superfamily that may play a role in muscle–fat interaction and muscle fiber growth. Among its various roles, it has been demonstrated to regulate metabolic diseases. According to a research study, *in vivo* administration of IL-15 increased glucose uptake in skeletal muscles, while *in vitro* IL-15 treatment increased glucose transporter type 4 mRNA content in C2C12 cells. These findings indicate that IL-15 may be an important regulator of muscle fiber growth, hypertrophy, and glucose uptake (Busquets et al., 2006). The most noticeable change in IL-15 was observed after moderate-intensity resistance training (Riechman et al., 2004). However, the results of those recent studies do not appear to be consistent. It is still unclear whether IL-15 increased through exercise and stimulated immunocytes to destroy cancer cells. However, in terms of metabolic regulation, it is clear that exercise can effectively mitigate metabolic diseases, including tumors, because it can develop skeletal muscle, a major site for insulin- and meal-dependent glucose disposal. Moreover, as past studies have consistently reported, cancer patients who underwent exercise rehabilitation showed enhanced immunocytes, such as natural killer cells, that help fight cancer cells. Therefore, a link may

exist between IL-15 and immunocytes substances.

Obesity, diabetes mellitus, and sarcopenia are risk factors in several types of cancer that may contribute to metabolic derangements often observed in cancer patients. Nevertheless, molecular and metabolic processes within skeletal muscle, adipose tissue, and the liver are markedly influenced by cancer. It is an apparent fact that exercise can reduce obesity and increase muscle mass. In other words, myokines such as IL-15 become active in healthy people who regularly exercise. In such individuals, immunocytes are secreted at appropriate times to help prevent and treat cancer cells. However, since this is only a theory, there is a need to investigate the specific basis regarding exercise rehabilitation for cancer patients. Exercise is a safe and effective method of intervention to improve metabolic health. Thus, it is a standard part of care for several lifestyle-related conditions, such as metabolic and cardiovascular disease. Exercise improves metabolic regulation via both acute events as well as chronic adaptations. Specifically, the longer-term benefits of regular exercise include increased insulin sensitivity, improved mitochondrial volume and function, and increased muscle mass and strength, thereby correcting the majority of metabolic dysfunctions caused by cancer.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

Busquets S, Figueras M, Almendro V, Lopez-Soriano FJ, Argiles JM. Interleukin-15 increases glucose uptake in skeletal muscle. An antidiabetogenic effect of the cytokine. Biochim Biophys Acta 2006;1760:1613-1617.

Kahn BB, Alquier T, Carling D, Hardie DG. AMP-activated protein kinase: ancient energy gauge provides clues to modern understanding of metabolism. Cell Metab 2005;1:15-25.

Pedersen BK. Muscles and their myokines. J Exp Biol 2011;214:337-346.

Pedersen BK, Febbraio MA. Muscles, exercise and obesity: skeletal muscle as a secretory organ. Nat Rev Endocrinol 2012;8:457-465.

Raun SH, Buch-Larsen K, Schwarz P, Sylow L. Exercise-a panacea of metabolic dysregulation in cancer: physiological and molecular insights. Int J Mol Sci 2021;22:3469.

Riechman SE, Balasekaran G, Roth SM, Ferrell RE. Association of interleukin-15 protein and interleukin-15 receptor genetic variation with resistance exercise training responses. J Appl Physiol 2004;97:2214-2219.

So B, Kim HJ, Kim J, Song W. Exercise-induced myokines in health and metabolic diseases. Integr Med Res 2014;3:172-179.

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