Letter to editor

Muscle-muscle crosstalk and potential therapies for muscle wasting diseases: does exercise matter?

Masoud Shabani[1], Mohammad Modirrousta[2], Hashem Shabdin[1], Zahra Sajadi[1], Elnaz Ghasemi[2], Faezeh Mohammadi[1*]

Dear Editor-in-Chief

Different types of exercise training with increasing muscle contraction can stimulate muscle secretome called myokines. Myokines are the main mediators of maintaining muscle structure and function in manner of autocrine and paracrine. These myokines can both affect distant tissues and have positive effects on muscle tissue itself (Chen, Wang, You, & Shan, 2021). In various diseases leading to muscle wasting, it seems that exercise and increased contraction can reduce the rate of muscle wasting and muscle atrophy by regulating myokines. Myostatin is a myokine that negatively regulates skeletal muscle development. In animal models, myostatin degradation has been shown to increase muscle mass and inhibit myostatin signals which can control the loss of muscle mass due to cancer cachexia (X. Zhou et al., 2010). Zhou et al. (2021) showed that exercise training (strength or balance in combination with endurance training) seems to be effective in preventing sarcopenia and maintaining muscle mass in non-dialysis-dependent patients with chronic kidney disease (CKD) with inhibition of myostatin signaling (Y. Zhou, Hellberg, Hellmark, Höglund, & Clyne, 2021).

Apelin is another myokine that decreases in age-dependent manner (Vinel et al., 2018). Apelin signaling in aging helps to increase muscle function by stimulating mitochondrial biogenesis and anti-inflammatory pathways in myofibers and improving regenerative capacity by targeting muscle stem cells (Vinel et al., 2018). It has been shown that exercise can positively regulate the Apelin and improve muscle growth. Apelin, an exerkine, is elevated due to maternal exercise, and maternal apelin administration mirrors the effect of maternal exercise on mitochondrial biogenesis in fetal muscle (Son et al., 2020). In other words, Apelin inhibits skeletal muscle dysfunction.

Leukemia inhibitory factor (LIF) is primarily expressed at low levels in type 1 muscle fibers. LIF has been shown to affect the growth and regeneration of skeletal muscle. For example, the expression of LIF protein in rat plantaris muscle is increased by mechanical load (Sakuma et al., 1998). Furthermore, LIF stimulates the hypertrophic response to increased load in the animal model, and in this respect LIF has been shown to be an important factor in skeletal muscle hypertrophy. In addition, LIF mRNA increases in human skeletal muscle following muscle damage leading to better repair. Therefore, this factor secreted by skeletal muscle can increase in various injuries and diseases with exercise and controls muscle wasting. Irisin is one of the most important muscle myokines that is secreted from muscle tissue through exercise and has auto and paracrine effects. It was shown that the injection of irisin induced muscle hypertrophy, improved muscle strength and reduced necrosis and development of connective tissue in a murine model (Reza et al., 2017). Therefore, increasing this factor with exercise can counteract cachexia and atrophy.

Musclin is an exercise-responsive myokine associated with plasma atrial NP (ANP) and cyclic guanosine monophosphate (cGMP) and the expression of the peroxisome proliferator-activated receptor γ coactivator 1-α (PGC1-α) expression in skeletal muscle after exercise training (Subbotina et al., 2015). Musclin helps increase exercise capacity by increasing mitochondrial biogenesis in mice (Subbotina et al., 2015). In addition to its role in exercise, Musclin reduces muscle tissue damage during the development of cachexia-induced tumors and has beneficial effects on cancer patients at risk for cachexia (Re Cecconi et al., 2019). C - X - C motif chemokine ligand 12 (CXCL12) is another type of myokine that is involved in the growth of skeletal muscle. CXCL12 helps proliferate myogenic and angiogenic somite progenitor cells and controls myotoma formation (Abduelmula et al., 2016). Moreover, it has been shown that the concentration of plasma CXCL12 is enhanced in response to training on a bicycle ergometer (Wang, Lee, Lien,

1. Department of Physiotherapy, School of Rehabilitation Sciences, Tehran University of Medical Sciences, Tehran, Iran. 2. Department of Physiotherapy, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran.

*Author for correspondence: fpt.mohammadi@gmail.com

M Sh: 0000-0002-1688-3931; M M: 0000-0003-1694-4105; H Sh: 0000-0003-0736-669X; Z S: 0000-0001-6778-3538; E Gh: 0000-0003-2519-676X; F M: 0000-0002-5504-3724

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& Weng, 2014). Overall, muscle - muscle crosstalk with several myokines mediates the beneficial effects of exercise training, including regulating muscle growth, preventing muscle loss, and increasing muscle function and regeneration, and these factors can decrease muscle wasting diseases.

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