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Letter to the Editor

MYOKINES IMMUNITY AND INFLAMMATION

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INTRODUCTION

Myokines described over the past decade are low molecular weight cytokines generated by skeletal muscle cells after muscular activity and secretion (1). Hence, the cytokines released by the muscles can be referred to as myokines. They can have local and systemic effects and can act like cytokines in an endocrine, autocrine, and paracrine manner (2, 3). These proteins act on many organs and tissues as their receptors are ubiquitous throughout the body. Myokines stimulate the protein kinase activated by AMP, increase glucose absorption, and improve lipolysis by demonstrating a therapeutic and preventive effect on metabolic diseases such as obesity (4, 5). During muscle exercise, myokines participate in tissue metabolic activity by regulating and protecting the physiological state of the muscle (7, 8). In addition, skeletal muscle carries out secretory activity, which is made up of many peptides, that allows it to crosstalk with other tissues (9, 10). Interleukin-6 (IL-6) can be considered a myokine that acts on the muscle, immune system, and liver. In arthritic pathologies, the liver produces serum proteins such as serum amyloid A (SAA) and fibrinogen, which are mediated by some cytokines, including IL-6 and IL-1. Liver cells cultured *in vitro* in the presence of IL-1 and IL-6 cause an increase in mRNA, proteins of the SAA and fibrinogen, a reaction that is inhibited by pretreatment with an IL-1 receptor blocker, such as interleukin-1 receptor antagonist (IL-1RA); this demonstrates that the SAA response in the acute phase requires inflammatory cytokines such as IL-1 and IL-6 (11, 12).

Exercise with muscle contractions causes physiological alterations by producing secretory molecules such as tumor necrosis factor (TNF) and chemokine CCL2 which can mediate obesity. The adipose tissue formed by adipocytes specifically produces leptin and inflammatory molecules that can transmit messages to the brain. Adipose tissue participates in the inflammatory process by producing adipokines which are in equilibrium with myokines (13, 14). Adipokines mediate inflammatory diseases such as atherosclerosis and diabetes, while myokines have beneficial effects on the human body. Therefore, skeletal muscle produces and releases myokines into blood circulation, opposing dysmetabolic phenomena such as diabetes and atherosclerosis and pro-inflammatory adipokines produced by adipose tissue. During physical ac-

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tivity, the muscle releases irisin, IL-15, leukaemia inhibitory factor (LIF), brain-derived neurotrophic factor (BDNF), fibroblast growth factor-21 (FGF-21), and SPARC, counteracting the synthesis of adipose tissue.
Myokines such as IL-6, IL-8, IL-15, IL-4, IL-7, myostatin, FGF, LIF, BDNF, erythropoietin (EPO), and brain-like growth factor insulin-1 (IGF-1) regulate the energy process by acting on carbohydrate and lipid metabolism and induce the production of biologically active molecules. Myokines protect us from cardiovascular diseases, obesity, and diabetes (15-18). The synthesis of myokines is reduced in physical inactivity, worsening the quality of life and the immune response. Physical exercise causes the synthesis of myokines, improving brain function. BDNF, upregulated by muscle-produced cathepsin B, is a well-studied myokine that regulates neurogenesis and synaptic function, although the exact mechanisms are still unclear. Skeletal muscle activity requires adenosine triphosphate (ATP), regulates myokine expression, increases oxidative stress, and mediates the neurobiological response. The production of myokines leads to an endocrine effect on metabolism, thermogenesis, inhibition of inflammation, mitochondrial biogenesis, and fatty acid oxidation. Myokines promote angiogenesis and represent a potential therapeutic target, although further investigation is needed.

CONCLUSION

In conclusion, myokines are a new class of functional molecules connected from a metabolic point of view to muscle, bone and adipose tissues and represent a new chapter in the physiology and pathology of human medicine.

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