Irisinemia: A Novel Concept to Coin in Clinical Medicine?

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Abstract

Skeletal muscle can express and release substances such as cytokines or other peptides capable of modulating metabolic processes. These cytokines, named 'myokines', function as hormones either locally within the muscle or by targeting distant organs. A novel peptidic myokine named 'irisin' has been recently identified. It has been noted that circulating irisin levels are lower in type 2 diabetes (T2D) compared with nondiabetic controls as well as in patients with chronic kidney disease. In addition, a negative correlation between the hemoglobin A1c (HbA1c) and circulating levels of irisin has been also observed. Thus, the blood concentration of irisin may reflect the metabolic status of patients suffering from metabolism disorders. In addition to glycemia or HbA1c, 'irisinemia' may also become a new promising concept employed to monitor metabolic disorders such as T2D or obesity, representing a novel and useful tool in the management of metabolic diseases in the near future.

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Increasing evidence demonstrates that skeletal muscle can express and release substances such as cytokines or other peptides capable of modulating metabolic processes. Therefore, skeletal muscle acts as an autocrine, paracrine, or endocrine organ, working in a hormone-like

model and thus exerting specific endocrine effects on other organs [1]. Accordingly, these cytokines are classified as 'myokines', which function as hormones either locally within the muscle or by targeting distant organs [2]. A physically active life plays an independent role in protection against metabolic syndrome, type 2 diabetes (T2D), and/or cardiovascular disease. Thus, induction of myokines by exercise has been suggested to prevent and/or improve several diseases [3]. In fact, lack of exercise is a major cause of chronic diseases such as sarcopenia, metabolic syndrome, obesity, insulin resistance, prediabetes, T2D, and others [4]. Skeletal muscle has the capacity to express numerous myokines (see table 1).

A novel peptidic myokine named 'irisin' was recently identified by Boström et al. [5]. Irisin is secreted in response to PPAR- γ coactivator-1 α (PGC-1 α) activation and acts on cells of white adipose tissue, promoting the acquisition of a brown adipocyte phenotype prone to energy expenditure [6]. Concentrations of irisin increase significantly after endurance exercise training in both mice and humans. Moreover, irisin levels in the blood are correlated with skeletal muscle irisin precursor FNDC5 mRNA levels. Irisin increases the total energy expenditure, prolongs life expectancy, reduces body weight, and mitigates diet-induced insulin resistance, thus reducing obesity and insulin resistance [5]. This underlines the im-

Table 1. Main myokines involved in the metabolism axis

Tumor necrosis factor- α (TNF- α)
Irisin
Interleukin-6 (IL-6)
Interleukin-8 (IL-8)
Interleukin-15 (IL-15)
Brain-derived neurotrophic factor (BDNF)
Leukemia inhibitory factor (LIF)
Fibroblast growth factor 21 (FGF21)
Follistatin-like-1
CXC motif ligand-1 (CXCL-1) also known as KC (keratinocyte-derived chemokine)

portance of exercise with regard to the overexpression of myokines [3]. More interestingly, it has been recently demonstrated that irisin is not only a myokine but also an adipokine [7]. It has also been noted that circulating irisin levels are lower in T2D compared to nondiabetic controls [8–10], as well as in patients with chronic kidney disease [11]. In addition, the FNDC5 gene also determines insulin sensitivity in humans [12]. Choi et al. [8] observed a negative correlation between hemoglobin A1c (HbA1c) and circulating levels of irisin. Furthermore, serum irisin concentrations are also negatively correlated with the body mass index (BMI) [9], and with the triglyceride contents in the liver and liver enzymes in obese adults [13].

Overall, the blood concentration of irisin may reflect the metabolic status of patients suffering from metabolism disorders. Although optimism should be guarded, the identification of irisin opens new possibilities because the application of irisin may prove beneficial not only in monitoring and/or treatment of obesity and diabetes [14] but also for a wide range of pathological conditions that are characterized by a variable imbalance of energy demand and expenditure [15, 16]. Interestingly, irisin levels can now be quickly and easily measured in human serum or plasma. In fact, laboratory assessment of irisin by commercial enzyme-linked immunosorbent assays (ELISA) is easily available. However, the poor standardization of methods, along with the often heterogeneous and discrepant results, shows that the validation of studies and ELISA kits in this field is mandatory. Finally, in addition to glycemia or HbA1c, ‘irisinemia’ may also become a new promising concept employed to monitor metabolic disorders such as T2D or obesity, representing a novel and useful tool in the management of metabolic diseases in the near future.

Disclosure Statement

The authors state that there are no conflicts of interest in the publication of this article.

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