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**Is Irisin a Miracle to Weight Loss?**

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## **Is Irisin a Miracle to Weight Loss?**

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### **Abstract**

Obesity is a worldwide health problem which causes serious metabolic disorders such as; insulin resistance, type 2 diabetes (T2D) and cardiovascular disease. It is described that obesity is a result of a chronic imbalance between energy intake and energy expenditure. The adipose tissue contains two functionally different types of fat: white and brown. White adipose tissue only stores fat, while the brown adipose produce heat as a defense against hypothermia and obesity. Brown adipose tissue affects whole-body metabolism and may alter insulin sensitivity and contribute to weight gain. Therefore, in general, antiobesity and antimetabolic disease therapy aims to enhance brown fat thermogenesis. Recent studies show that white adipose tissue can be converted to thermogenically active beige adipose tissue via a novel hormone, irisin. It is thought that Irisin basically acts on the cells of white adipose tissue. After exercise concentration of the irisin increase in mice, thus increasing total energy expenditure and alleviating diet induced insulin resistance in animal models.

A recent study by Boström and colleagues reported that expression of the exercise- and PGC-1 $\alpha$ -induced hormone, irisin, promotes the conversion of white fat to brown fat in mice and humans. These reviews indicate that exercise regulates the expression of irisin in muscle. Thus exercise gives the benefits on metabolic disorders and energy homeostasis.

**Keywords:** Irisin, exercise, obesity

## **Introduction**

Boström and colleagues have discovered a new protein of 112 amino acids that is named irisin. Irisin is produced from Fndc5 in the muscle and works on white adipose tissue to make it brown, causing increased energy expenditure which in turn reduces obesity. Irisin is secreted during exercise and overexpression of irisin results with an increase in UCP-1 and improvement in glucose homeostasis.(Boström et al.,2012; Huh et al., 2012) This review indicate that irisin is a protein secreted by myocytes by exercise on energy balance and metabolic disorders such as type 2 diabetes mellitus, obesity, metabolic syndrome. Although much work is still needed, irisin is being applied currently in the treatment of obesity.

## **Obesity and Adipose Tissues**

Obesity is a worldwide health problem which triggers the development of insulin resistance, type 2 diabetes (T2DM) and cardiovascular disease (Choi et al., 2013). According to data from world health organization;

- “a. worldwide obesity has nearly doubled since 1980.
- b. In 2008, more than 1.4 billion adults were overweight. Of these over 200 million men and nearly 300 million women were obese.
- c. 35% of adults aged 20 and over were overweight in 2008, and 11% were obese.
- d. 65% of the world's population live in countries where overweight and obesity kills more people than underweight.
- e. More than 40 million children under the age of five were overweight in 2011.” (WHO, 2013)

We can simply define obesity as the result of a chronic imbalance between energy intake and energy expenditure. Currently, the mechanisms of energy expenditure is not clear yet (Swick, 2013). Boosting the energy consumption is an important part of combating metabolic disorders such as obesity, type 2 diabetes and metabolic syndrome (Wu and Spiegelman, 2014). Epidemiological studies have revealed that there is a strong relationship between obesity and physical inactivity. These studies show the benefits of exercise on obesity (Ciolac and Guilherme 2004). For the treatment of obesity, it is required that the energy expenditure be higher than the daily energy intake. Therefore, increasing the amount of physical activity with exercise is the best treatment (Ciolac and Guilherme 2004).

Exercise is a major factor of healthiness. Recent studies have demonstrated that exercise also causes an increase in energy expenditure through enhancement in brown fat and the browning of white fat (Wu and Spiegelman, 2014). Brown adipose tissue (BAT) oxidizes chemical energy to produce heat as a defense against hypothermia and obesity (Choi et al., 2013). Brown

adipose cells have a ultra mitochondrial content and also express uncoupling protein 1 (UCP1). Therefore they deploy chemical energy in the form of heat (Wu and Spiegelman, 2014). As mentioned before, BAT contributes to energy expenditure through deploying energy as heat and can thus fight weight gain. Brown adipose cells have numerous mitochondria. As it is known, mitochondrias of brown adipose cells contain a unique protein called uncoupling protein 1 (UCP1) (Seale and Lazar, 2009). UCP1 acts as a proton carrier activated by free fatty acids and creates a shunt between complexes of the respiratory chain and ATP synthase. Activation of UCP1 enhances respiration. This process results in dissipation of oxidation energy as heat (Rousset et al., 2004). Transcriptional control of brown fat cell fate, is an important and attractive subject. For instance, Zinc finger transcriptional regulator PR domain containing 16 (PRDM16) has recently revealed as a strong regulator of brown fat cell fate (Seale and Lazar, 2009). Also several polypeptides have browning effects, such as FGF21, BNP/ANP, BMP7 and orexin (Wu and Spiegelman, 2014). The regulation of BAT in humans is not fully understood. However, a recently found peptide may influence the regulation of energy expenditure (Swick, 2013).

### **Focus on Irisin**

Böstrom and et al. reported that overexpression of PGC1- $\alpha$  in mice induced the expression of the FNDC5 gene in muscle. FNDC5 encodes a type 1 membrane protein that is proteolytically cleaved to produce a secreted plasma hormone named irisin (Swick, 2013).

Importantly, this causes a significant increase in total body energy expenditure and resistance to obesity-linked insulin resistance

Irisin is a new hormone which was recently identified by Boström et al. in 2012. The hormone is secreted by myocytes which acts on the white adipose tissue (Sanchis-Gomar et al., 2012; Huh et al. 2012). This hormone is induced by Peroxisome proliferator-activated receptor (ppar)- $\gamma$  coactivator (PGC1- $\alpha$ ). PGC-1- $\alpha$  is a transcription coactivator. PGC1-a stimulates the secretion of several skeletal muscle factors including Fibronectin type III domain-containing 5 protein (FNDC5) (Boström et al, 2012). Boström and colleagues found that exercise induced the expression of the Fndc5 gene in skeletal muscle of both mouse and human (Erickson, 2013). They later used adenovirus to overexpress full length FNDC5 in the liver of mice. They found a stunning increase in brown adipose tissue of the FNDC5-expressing mice. Boström et al. proposed that an protease breaks down the ectodomain of FNDC5, producing the soluble irisin protein (Erickson, 2013).Boström and colleagues showed that muscle-specific knockout of PGC1- $\alpha$  decreased irisin levels by 72%. In their study they also implemented exercise programme to mice via free wheel running for 3 weeks, after 3 weeks of exercise programme, plasma irisin levels had increased by 65% in mice.In the same way plasma irisin levels were found to double in healthy humans after 10 weeks of endurance exercise (Castillo-

Quan, 2012). Based on these studies they have also proved the positive effects of exercise on plasma irisin levels (Castillo-Quan, 2012). According to data from Choi and colleagues's study, irisin can be used to treat type 2 diabetes and insulin resistance. Irisin levels have been reported to increase with exercise and to be lower in patients with type 2 diabetes (Swick, 2013; Choi et al., 2013).

Based on these data irisin administration can be a potentially striking future therapeutic target for metabolic disorders (Huh et al., 2012).

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