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The role of irisin in ischemic heart disease

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Abstract:

Introduction: Physical effort has a positive effect on the human body, through its protective effect on the development of many diseases, along with cardiovascular system diseases. Irisin is an adipomiokine that is a fragment of the doemeny of extracellular FNDC5 protein.

It is released from FNDC5 due to physical activity and peroxisome proliferator receptor-γ coactivator 1α (PGC-1α) stimulation. It forms a link between the muscles and other tissues of the body. Moreover, it affects the conversion of white adipose tissue into brownish-like fat tissue.

Aim: For over 15 years ischemic heart disease has been one of the most common causes of death in the world. Therefore, attempts have been made to clarify the role it has in ischemic heart disease.

Conclusions: It has been proven, that the concentration of irisin decreases in patients with myocardial infarction it also correlates with the severity of stable coronary disease and a higher SYNTAX score. Hence, the hypothesis was that the level of this protein probably depends on the inflow of blood to the myocardium. It can therefore be used for the panel of myocardial damage. The New Approach of therapeutic options uses irisin with stem cells during the repairing of myocardium. Despite much interest in irisin, there are still many questions that need to be answered, in particular those related to the irisin cell receptor and what is related to the clarification of its mechanisms in physiology.

Introduction and aim:

Physical effort has a beneficial effect on the human body, through its protective effect on the development of many diseases, along with cardiovascular system diseases. Therefore, for years, researchers have tried to discover an element that connects muscles with other tissues of the human body. The results of the study have reported the existence of a protein that influences metabolism and importantly, that secreted by skeletal muscle after physical exertion. The protein was named irisin, after the Greek goddess Iris, the mythological messenger of the Olympic gods. Irisin is an adipomiokine that is a fragment of the doemeny of extracellular FNDC5 protein. It is released from FNDC5 due to physical activity and stimulation of peroxisome proliferator receptor-γ coactivator 1α (PGC-1α), molecules affecting energy metabolism. It is worth noting that when PGC-1α expression is increased, mitochondrial biogenesis occurs, the formation of neuromuscular junction increases, angiogenesis is stimulated, and glucose-dependent uptake of glucose increases. Irisin is involved in the conversion of white adipose tissue into the so-called beige tissue, which builds and functions like brown adipose tissue responsible for mindless thermogenesis and counteracting obesity. Some of the first research models for this molecule were carried out on mice. In their subcutaneous adipose tissue, an increase in mRNA expression for thermogenin was demonstrated. Thermogenin is a protein characteristic of brown adipose tissue and responsible for heat production by uncoupling the respiratory chain in the mitochondria. The start codon of the FNDC5 gene is different in mice and humans. This may be the reason for the functional and antigenic difference between mouse and human irisin. The irisin cell receptor is also unknown. It is suggested that this is a surface receptor, because irisin is characterized by a rapid duration of action. Identifying this receptor is important in understanding its mechanism in physiology [1]. So far the most popular studies focused on looking for links between levels of irisin in the blood serum

and the occurrence of individual disease entities. It's aim was to influence the widening of the diagnostic and possibly therapeutic panel.

For over 15 years ischemic heart disease has been one of the most common causes of death in the World [2]. Therefore, many researchers decided to answer the question - what role does irisin play in ischemic heart disease?

Developing:

Already in 2014, irisin was described as a potential marker of myocardial infarction. The study was performed on rats to which myocardial infarction was induced with isoproterenol and the expression of irisin in the heart, skeletal muscle, kidneys and liver was immunohistochemically determined and the irisin level in the blood serum was determined by enzyme-linked immunosorbent assai (ELISA). Regardless of the time, the level of irisine increased near the connective tissue of the myocardium. In skeletal muscle, liver and kidneys, irisin production increased after 6 hours, although slower than in the controled group alone. Hence the hypothesis that the gradual reduction in the level of this protein may be a diagnostic marker of myocardial infarction [3].

Another milestone has been to prove that healthy centenarians are characterized by increased levels of irisin in the blood serum. In young patients with myocardial infarction, the level of this molecule turned out to be much lower. This discovery led to further attempts to determine the effects of irisin not only in vascular disorders, but also in modulation of life expectancy [4].

Two years later, it was described that irisin significantly reduces atherosclerosis in mice deficient in apolipoprotein E, which is a hydrophilic component of such lipoproteins as: high density lipoprotein (HDL), very low den sity lipoprotein (VLDL), chylomicrons. Irisin promotes proliferation of endothelial cells by mikroRNA126-5p, thereby reducing atherosclerosis. However, it was still intensively sought for its direct therapeutic effect on atherosclerotic diseases [5].

The results of the first study, which showed that lowered levels of irisin are predicting the severity of stable coronary disease and a higher score on the SYNTAX scale (tools for angiographic assessment determining the complexity of coronary heart disease), were presented in 2017 [6].

In the same year, the results of analyzes were also published, which focused not only on irisin, but also on follistatin and activin A. Folistatin is a protein that binds and inhibits the action of activin A, which in turn belongs to the family of transforming growth factors β. Circulating irisin concentrations were found to be lower in patients with stable coronary

disease or miocardial infarction compared to healthy controls. However, levels of follistatin and activin A were higher in patients with myocardial infarction. Their values were so significant that they made it possible to distinguish between myocardial infarction and stable coronary disease with an accuracy similar to creatine kinase muscle-brain (CK-MB). This suggests their increased release due to myocardial necrosis. Irisin levels were lower in myocardial infarction and stable coronary heart disease. It is therefore assumed that their production may depend on the inflow of blood to the myocardium [7].

Also in 2017, the results of a large analysis of case-control studies were published, in which the relationship between the concentration of irisin and the occurrence of coronary heart disease was described. The publications from the years 2000-2017 were analyzed, which were in the PubMed, Medline, Elsevier Science Direct, Springer, Web of Science and China National Knowledge Infrastructure databases. It was confirmed that the level of irisin was significantly lower in patients with coronary artery disease [8].

In the following year (2018) an attempt was made to clarify the role of irisin in cardiac surgery. A useful parameter in monitoring coronary coronary bypass surgery is the measurement of irisine concentration with lactate. It was interesting, that the level of irisin also changed during hypothermia. Useful parameters for myocardial damage panel may be (outside CK-MB, troponin T (TnT) and type B naturopuretic peptide (BNP)) measurements of irisine concentration [9].

Another important aspect was the presentation that irisin concentration changes significantly after myocardial infarction with ST elevation (STEMI) and is associated with adverse cardiovascular consequences after myocardial infarction. In a prospective, single-center cohort study, irisin concentrations were measured using an enzyme-linked immunosorbent assay. The studies were performed in 399 patients 28 days after the onset of STEMI, which then was followed for 3 years to assess the relationship between irisin concentrations and adverse cardiovascular events. These events included: excessive risk of death due to cardiovascular causes, stroke, and heart failure. These events were mainly observed in people with the highest concentrations of irisn. Importantly, up to a 4-fold increase in risk occurred at concentrations higher than the 75th percentile of total distribution. The results showed that serum irisin concentrations were elevated in STEMI patients with an increased risk of adverse cardiovascular events [10].

The most recent study of 2019 describes irisin as a factor that supports myocardial repair when induced by progenitor cells, which in turn leads to improved heart function after a heart attack. The study was performed on mice in which the infarction was induced by permanent ligation of the left anterior descending artery. Then, progenitor cells were introduced that were previously isolated from mouse embryonic stem cells and pre-treated with irisin 24 hours before transplantation. After 8 weeks, the functions of the myocardium were evaluated using echocardiography. As a result, there was an improvement in ventricular function (as evidenced by an increase in ejection fraction) and a reduction in myocardial hypertrophy and interstitial fibrosis was observed. Transplantation of mouse embryonic stem

cells promoted myocardial regeneration and neovascularization, which further increased after treatment in combination with irisin. Such treatment promoted proliferation of myocytes. Proof of that were proliferation markers and reduced apoptosis. Irisin was responsible for heart regeneration and functional induction of embryonic stem cells. This molecule can therefore serve as a new therapeutic approach for stem cells in the repair of the myocardium [11].

Summary:

Year by year, knowledge about irisin is growing. This is adipomikine with which high hopes are associated. Some of the questions have been answered, many still need verification or further research - in particular, the identification of the cellular receptor for irisin, which may allow to refine its mechanisms of action in physiology. The results obtained from rodent studies are consistent and suggestive. Discrepancies arise when research is carried out on people. The start codon of the FNDC5 gene is different in mice and humans, it may be the reason for the functional and antigenic difference between mouse and human irisin. [1] However, in association with ischemic heart disease, it has been proven that the concentration of irisin decreases in patients with myocardial infarction, and its low level also correlates with the severity of stable coronary disease and higher SYNTAX score [4,6,7,8]. Hence the hypothesis that the level of this protein probably depends on the inflow of blood to the myocardium[7]. It can therefore be used for the panel of myocardial damage [9]. In turn, in 2018, the results of a cohortal, prospective, single-center study showed that high levels of irisn were correlated with the increased risk of adverse cardiovascular events in patients with ST-segment elevation myocardial infarction. [10] In terms of therapeutic options, irisin in the repair of myocardium using stem cells may be a new approach [11]. Certainly, irisin studies are worth further investigation, because of the potential benefits that they can bring both at the diagnostic and therapeutic levels.

Bibliography:

1. Pukajło K., Kolackov K., Łaczmańsk Ł., Daroszewski J.: Irisin – a new mediator of energy homeostasis. Advances in Hygiene and Experimental Medicine. 2015; 69: 233-242.
2. World Health Organisation. The top 10 causes of Heath [online]. WHO. [Przeglądany 24 czerwca 2019]. Dostępny w: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death.
3. Kuloglu T., Aydin S., Eren M.N., Yilmaz M., Sahin İ., Kalayci M., et al.: Irisin: A potentially candidate marker for myocardial infarction. Peptides. 2014. 55:85–91.

4. Emanuele E., Minoretti P., Pareja-Galeano H., Sanchis-Gomar F., Garatachea N, Lucia A. :Serum Irisin Levels, Precocious Myocardial Infarction, and Healthy Exceptional Longevity. Am J Med. 2014. 127(9):888–90.
5. Zhang Y., Song H., Zhang Y., Wu F., Mu Q., Jiang M., et al.: Irisin Inhibits Atherosclerosis by Promoting Endothelial Proliferation Through microRNA126-5p. J Am Heart Assoc. 2016. 5(9).
6. Efe T.H., Açar B., Ertem A.G., Yayla K.G., Algül E., Yayla Ç., et al. Serum Irisin Level Can Predict the Severity of Coronary Artery Disease in Patients with Stable Angina. Korean Circ J. 2017.47(1):44.
7. Anastasilakis A.D., Koulaxis D., Kefala N., Polyzos S.A., Upadhyay J., Pagkalidou E., et al.:Circulating irisin levels are lower in patients with either stable coronary artery disease (CAD) or myocardial infarction (MI) versus healthy controls, whereas follistatin and activin A levels are higher and can discriminate MI from CAD with similar to CK-MB accuracy. Metabolism. 2017.73:1–8.
8. Guo W., Zhang B., Wang X.: Lower irisin levels in coronary artery disease: a meta-analysis. Minerva Endocrinol. 2017.
9. Aydin S., Catak Z., Eren M.N., Topal A.E., Aydin S.: Irisin in Coronary Bypass Surgery. Cardiovasc Hematol Disord Targets. 2018.18(3):208–14.
10. Hsieh I.C., Ho M.Y., Wen M.S., Chen C.C., Hsieh M.J., Lin C.P., et al.: Serum irisin levels are associated with adverse cardiovascular outcomes in patients with acute myocardial infarction. Int J Cardiol. 2018 . 261:12–7.
11. Zhao Y.T., Wang J., Yano N., Zhang L.X., Wang H., Zhang S., et al.: Irisin promotes cardiac progenitor cell-induced myocardial repair and functional improvement in infarcted heart. J Cell Physiol. 2019. 234(2):1671–81.