ISSN: 2181-3337 SCIENCE AND INNOVATION
INTERNATIONAL SCIENTIFIC JOURNAL
2022 № 4

ENZYMATIC SYSTEM OF PROTECTION AGAINST OXIDATIVE STRESS

Nargiza Hamzayeva
Assistant teacher, Department of Physiology, Faculty of Chemistry and Biology, Karshi state university
Nargiza Yoqubova
Student, Department of Physiology, Faculty of Chemistry and Biology, Karshi state university

https://doi.org/10.5281/zenodo.6832490

Abstract. *Sirtuin genes are reported to act as sensors that detect the availability of cellular energy, leading to metabolic benefits, as calorie restriction prolongs life expectancy in organisms ranging from yeast to mammals. It has been shown that the mammalian orthologue Sir2, SIRT1 (sirtuin 1), activates a critical component of calorie restriction in mammals, that is, fat mobilization in white adipocytes. Recent studies suggest a key role of mammalian SIRT1 in an adequate cellular response to metabolic stress, such as nutrient deficiency or overload, and that SIRT1 and its activators play a role in protecting against the harmful effects of metabolic stressors.*

Key words: *sirtuin, ROS productions, antioxidants, oxidative stress, metabolis.*

ФЕРМЕНТАТИВНАЯ СИСТЕМА ЗАЩИТЫ ОТ ОКСИДАТИВНОГО СТРЕССА

Аннотация. *Сообщается, что гены сиртуина действуют как датчики, которые обнаруживают наличие клеточной энергии, что приводит к метаболическим преимуществам, поскольку ограничение калорий увеличивает продолжительность жизни в организмах, начиная от дрожжей и заканчивая млекопитающими. Было показано, что ортолог Sir2 млекопитающих, SIRT1 (сиртуин 1), активирует критический компонент ограничения калорий у млекопитающих, то есть мобилизацию жира в белых адипоцитах. Недавние исследования предполагают ключевую роль SIRT1 млекопитающих в адекватном клеточном ответе на метаболический стресс, такой как дефицит питательных веществ или перегрузка, и что SIRT1 и его активаторы играют роль в защите от вредного воздействия метаболических стрессоров.*

Ключевые слова: *сиртуин, продукция АФК, антиоксиданты, окислительный стресс, метаболизм.*

INTRODUCTION

A key role in the regulation of adipogenesis is played by the nuclear receptor PPAR-γ (a receptor activated by the proliferator peroxisome-gamma). Indeed, when refusing food, the SIRT1 protein binds and suppresses genes controlled by the fat regulator PPAR-γ, including genes mediating fat accumulation. SIRT1 represses PPAR-γ by docking with its cofactors NCoR (nuclear receptor corepressor) and SMRT (retinoid and thyroid hormone receptor silencing mediator). The mobilization of fatty acids from fasting white adipocytes is disrupted in SIRT1 (+/-) mice. In differentiated fat cells, increased regulation of SIRT1 triggers lipolysis and fat loss (Picard F, 2004). Since the reduction in fat content is sufficient to prolong the life of mice, the above results provide a possible molecular pathway linking calorie restriction with life extension in mammals.

RESEARCH METHOD AND METHODOLOGY

In a study using liver-specific SIRT1 knockout mice, some challenge the assumption that calorie restriction always activates SIRT1 in all tissue types, demonstrating that SIRT1 activity decreases in the liver during calorie restriction, but is activated when mice are fed a high-calorie diet (Robert Fried, 2018). The study showed that liver-specific SIRT1 knockout mice have at least some protection, compared to wild-type mice, from fat accumulation during a high-calorie diet. In contrast, under calorie restriction, liver-specific knockout rats have the same phenotype. These observations suggest that hepatic SIRT1 can be inactivated during calorie restriction in normal mice and activated during a high-calorie diet, unlike what happens in muscles and white adipose tissue, which can be explained by the different redox status and the ratio of NAD/NADH in the liver from other tissues in the study conditions. This may raise the interesting possibility that SIRT1 inhibitors specifically targeted at the liver may be useful in the treatment of obesity (Danika Chen, 2008). The concept that SIRT1 activation can lead to fat loss without affecting calorie intake may open the door to new treatments for obesity and related diseases. In addition, sirtuin can be considered a promising biomarker for determining the nutritional status in terms of fat accumulation and oxidation, and its modulation will have a beneficial effect on the accumulation and metabolism of fat in the body. The effect of sirtuin on overall metabolism is multidimensional, and its metabolic functions show that their effect on degenerative diseases is extremely important. Sirtuins also affect the immune system by reducing inflammation in many tissues, especially in macrophages, whereas a decrease in SIRT1 in liver cells leads to increased local inflammation. Some scientific articles have shown that mice fed a high-fat diet with the introduction of SIRT1 improved liver function and metabolism.

RESEARCH RESULTS AND DISCUSSION

In the brain, SIRT1 functions as a potential link between pituitary hormones and longevity pathways in calorie restriction in mammals. Many changes caused by sirt1 activation are associated with increased mitochondrial metabolism and antioxidant protection in starving fish (Baur, 2010). It is worth noting that overexpression of SIRT1 suppressed pro-inflammatory genes in mice, whereas obesity with chronic inflammation was associated with a decrease in SIRT1 levels. This discovery confirms and highlights the ability of sirtuin as a biomarker of inflammation caused by the accumulation of lipids in biological systems. Members of the sirtuin family, which are NADC-dependent deacetylases, are involved in many cellular processes, such as cell proliferation, aging, and stress response (Shin-Hae Lee, 2019). They can play either a stimulating or suppressive role, depending on the organ or even the species. SIRT1 expression increases in prostate cancer and acute myelocytic leukemia (DENG-FENG YU, 2016). There was an increased overexpression of sirt1 in the adenoma of the thick tubules, and it was recommended as a useful biomarker in the diagnosis of high-grade dysplasia and invasive carcinoma. Another group of researchers noticed that the activity of SIRT1 and SIRT2 proteins was significantly increased in lung cancer cell lines compared to non-tumor lung epithelial cells (Ivana Grbesa, 2015). It was also found that the expression of sirt1 and SIRT2 proteins increases in lung tumor cells compared to normal lung cells. These results even suggest that SIRT1 inhibitors may act as potential antitumor agents and that when considering SIRT1 inhibitors for cancer treatment, the potential tumor suppressing effects of SIRT1 should be taken into account. There are many studies that have demonstrated that a possible mechanism for the regulation of SIRT1 on the cancer gene is associated with the tumor protein p53. P53 protein is known to be a

tumor suppressor protein (Mohammad Athar, 2011). Its reduced expression or mutation leads to an increased risk of developing cancer. It is reported that the deacetylation of p53 SIRT1 plays an important role in preventing the activation of p53 and thus contributes to the development of cancer (Fang, 2013). This is how SIRT1 affects the activity of the p53 gene and stands out as an agent contributing to the development of cancer. But there is a significant paradox in this regard. Several controversial studies have shown that p53 SIRT1 inactivation actually promotes cell survival during stress and that SIRT1 stops p53-induced apoptosis by deacetylation of p53 and induction of manganese superoxide dismutase. Despite the clear inhibitory effect of increased SIRT1 expression on tumor suppressors such as p53, other studies have shown that SIRT1 may also have tumor suppressing functions (Jingjie Yi 1, 2010). This can be partly explained by studies conducted where they observed that SIRT1 provides protection against oxidative stress by modulating fork head transcription factors in some cells. Although researchers have noticed that SIRT1 protects cells from oxidative stress by increasing the activity of the antioxidant enzyme catalase (Antero Salminen, 2013). Calorie restriction helps to combat oxidative stress due to SIRT3-mediated enhancement of superoxide dismutase (SOD) activity. In addition, overexpression of SIRT1 increases resistance to free radical toxicity in neuronal cells. Some studies of polyphenols have reported that they increase the chances of cell survival by stimulating SIRT1-dependent deacetylation of p53 (Konrad T Howitz 1, 2003).The expression and activation of SIRT1 can be influenced by several cellular conditions, such as calorie restriction, exercise, and oxidative stress in the cell. SIRT1 uses NADC as a substrate, but the NADC level can also control the deacetylating activity of SIRT1. Moreover, the activity of SIRT1 may depend on the cellular process and the cell type being studied. Thus, is it reasonable to assume that the level of sirtuin increases during cancer as part of the body's homeostasis and performs a protective mechanism to fight cancer and induces longevity in the form of sirtuins. This aspect of research is rife with contradictions and bi-directional views, so it needs more attention and understanding to actualize the role of sirtuin in degenerative diseases. SIRT4 has been found to modulate the metabolism of non-esterified (“free” or unsaturated) fatty acids (NEFA) (Frank K. Huynh, 2018). Adipose tissues secrete NEFA, causing oxidative stress, which leads to endothelial dysfunction, early atherosclerosis, which leads to risk factors for coronary heart disease. A decrease in SIRT4 activity was associated with increased oxidation of free fatty acids in the liver and muscles (Yumei Han, 2019). This discovery indicates that an increased level of SIRT4 can be considered as an indicator of an improvement in the antioxidant status of the body in terms of NEFA concentration. Studies have shown that sirtuin reduces reactive oxygen species (ROS) by modulating the acetylation of the respiratory chain, stimulating mitochondrial SOD and isocytrium dehydrogenase, which generates NADPH for the glutathione pathway (A. Y. Andreev1*, 2015). Such reports confirm the significant antioxidant potential of sirtuins, and they have shown that all seven sirtuins are found within detectable limits in all human tissues, moreover, the effect of sirtuin on most tissues can be traced, so we must establish the metabolomics performed by sirtuins and study it in detail.

Reactive oxygen species (ROS)

Reactive oxygen species (ROS) were initially recognized as toxic by-products of aerobic metabolism. In recent years, it has become apparent that ROS play an important signaling role in plants, controlling processes such as growth, development, and especially the response to biotic

and abiotic environmental stimuli. The main members of the ROS family include free radicals such as O2, OH•, and non-radicals such as H2O2 and 1O2 (Roychoudhury*, 2014). ROS production in plants is mainly localized in chloroplasts, mitochondria and peroxisomes. There are also secondary sites such as the endoplasmic reticulum, cell membrane, cell wall and apoplast. The role of the ROS family is a double-edged sword; while they act as secondary intermediaries in various key physiological phenomena, they also cause oxidative damage under various stressful environmental conditions, such as salinization, drought, cold, heavy metals, ultraviolet irradiation, etc., when the delicate balance between production and the elimination of ROS, which is necessary for normal cellular homeostasis, is disrupted. Cell damage manifests itself in the form of degradation of biomolecules such as pigments, proteins, lipids, carbohydrates and DNA, which eventually combine into the cellular death of plants.

CONCULISION

To ensure survival, plants have developed an effective antioxidant mechanism consisting of two branches, (i) enzymatic components such as superoxide dismutase (SOD), catalase (CAT), ascorbate peroxidase (APX), guaiacol peroxidase (GPX), glutathione reductase (GR), monodehydroascorbate reductase (MDHAR) and dehydroascorbate reductase (DHAR); (ii) non-enzymatic antioxidants such as ascorbic acid (AA), reduced glutathione (GSH), α-tocopherol, carotenoids, flavonoids and osmolite proline. These two components work hand in hand to remove ROS. In this review, we pay special attention to various types of ROS, their cellular production sites, their targets, and the mechanism of their absorption mediated by both branches of antioxidant systems, emphasizing the potential role of antioxidants in abiotic stress resistance and cell survival. Such comprehensive knowledge of the action of ROS and their regulation on antioxidants will allow us to develop strategies for genetic engineering of stress-resistant plants.

REFERENCES

1. P, K. S. (2019). *Cold Atmospheric Plasmas: Their Use In Biology And Medicine.* Science
2. P.Sachdevae, T. A. (2013). The role of polyphenols in the modulation of sirtuins and other pathways involved in Alzheimer's disease. *Ageing Research Reviews*, 867.
3. Pang, M. S.-G. (2019). Understanding the molecular mechanisms of bisphenol A action in spermatozoa. *Clin Exp Reprod Med.*
4. Patel SA1. (2014). Transcriptional control of antioxidant defense by the circadian clock. *Antiox redox signaling*, 20(18):2997-3006.
5. Paul S. Cooke, .. N. (2013). Safety Assessment including Current and Emerging Issues in Toxicologic Pathology. *Haschek and Rousseaux's Handbook of Toxicologic Pathology (Third Edition)*.
6. Paul∗, M. D. (2019). Gallic acid protects rat liver mitochondria ex vivo from bisphenol A induced oxidative stress mediated damages. *Toxicol Rep*, 6: 578–589.
7. Roychoudhury*, K. D. (2014). Reactive oxygen species (ROS) and response of antioxidants as ROS-scavengers during environmental stress in plants. *Front. Environ. Sci.*