Heat Shock Proteins (HSPs): a Review

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Abstract
Heat shock proteins (HSPs) are a large class of proteins that have been conserved throughout evolution and exist by prokaryote and eukaryote organisms. Heat shock proteins play an important role in protein homeostasis. They can found in all major cellular compartments. The HSP90 family are important in the formation of the steroid receptor complex. The HSP70 family is necessary for protein synthesis, translocation, and folding. HSP60 family is important in protein stability. Many factors, e. g. heavy metals and organic toxic substances, elevated temperature in all cells responsive to the formation of proteins called stress proteins. This is happening with a simple bacterium and with complex of neurons too. The concentration of HSPs in muscle in young and adults birds is increasing rapidly in the cellular stress. Increasing HSPs leads to significant changes in gene expression, which lead to reconstruction of skeletal muscle.

Keywords: chaperone, expression, stress, high shock protein

1. Introduction

P. Paulov laid foundations of experimental investigation of physiological changes in organisms of animals following exposure to stress factors. Cannon studied animals under stress that are exhibited excessive cold, heat or noise. He discovered the importance of the so-called. sympathoadrenal system in stress, which corresponds for a human natural defense the imminent danger "fight or flight". The concept followed H. Cannon Selye. He is considered the founder of the so-called corticoid idea of stress, which means that the important role played during stress increased function of adrenal glands [1].
Hladký [2] differentiated the physiological and the psychological stress.
The physiological stress is characteristic the vegetative and neurohumoral physical reactions to the noxious stimulus factors, ie., disturb, or hurt tissue structure or function [3].

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Stress can triggered with impulses from the external environment, but also with signals from the internal environment [4].
Schreiber [3] identified the psychological and somatic stressors (causes, factors). In the somatic stressors are environmental physical effects (cold, heat, different types of radiation, atmospheric pressure changes, noise, vibration), and somatic pathologies (hunger, thirst, pain, immobilization, bleeding, exercise, surgery). Schreiber classified the psychological stressors as conflict, frustration, unhealthy lifestyle, mental fatigue, pain, worry, interpersonal conflicts, work overload and others.
Each stress has the effect of activation of neuroendocrine system, particularly the hypothalamic - pituitary - adrenal glands and sympathetic nervous system. However, if the stressors that central and peripheral nervous system is unable to detect, the mechanism must be involved in the immune system. The cells registering in the body the presence of bacteria, viruses, tumor antigens and others uncognitive stressors against which induce an immune response. Cells produce not only antibodies, but also cytokines, prostanoids, neuroendocrine

hormones and other mediators during their immune response. They act locally, or activate the neuroendocrine system and sympathetic nervous system. The result of this activation is enhanced production adrenocorticotropin hormone, endorphins, glucocorticoids and catecholamines. All of them have strong immunosuppressive effect. In this mechanism, the immune system uses some hormones and neurotransmitters such as feedback molecules to regulate and termination its specific activity [5].

A number of factors, for example, heavy metals and organic toxic substances increased temperature in all cells, from simple bacteria and ending with complex neurons respond to the formation of proteins they are called stress proteins. They are emerging in injured cells cultured in a test tube, the cells of Drosofiles exposed to high temperatures, in the tissues of children with fever, in people's bodies after a heart attack and cancer patients receiving chemotherapy. Genes that encode the production of stress proteins are more than 50% identical in bacteria, yeast, fruit fly - Drosofile. Stress proteins have basically similar biologically important roles in all organisms [6].

When normal cells exposed to heat, the cells begin to intensively synthesize stress proteins, heat shock proteins (HSPs, heat-shock proteins) that have chaperone function. They are therefore called chaperones [7].

Chaperones regulate changes in the protein arrangement through membranes during transport. They regulate conformation - arrangement of proteins at the slight damage [8].

Later studies demonstrated the presence of molecular chaperones in the folding of new synthesized proteins they participate in their transport across membranes, as well as their integration into various organelles [9].

Chaperones inhibit of change of proteins conformation at increased temperature to 42 °C in the cell. The cell can adapt and range of this adaptation is limited and the cell is damaged by the intense stress [7].

Molecular chaperones have important functions in maintaining cell homeostasis and the cellular response to stress. Specifically, the following various properties and functions:

• they prevent the proteins aggregation in folding and unfolding of protein,

• has affect the production and kinetics in protein folding,

• are involved in the transfer of cellular proteins between compartments,

• have a regulatory function in signal transduction [10].

Stress proteins include molecular chaperones and proteins induced by high temperatures and also proteases, ubiquitin and dehydrins. Increase expression of HSPs is going in living organisms by sudden increase in ambient temperature above the optimum growth temperature [11].

The presence of HSPs was demonstrated in all living organisms. It is synthesized as a response to other stress factors such as cold, UV radiation [12], bacterial and viral infections [13], heavy metals [14], pesticides [15] and others.

Activation of HSPs genes is a universal answer to cell stress caused by high temperature, but also radiation, oxidative damage, heavy metal and it includes changes in transcription and translation. The answer by thermal shock is an important homeostatic mechanism that allows for bacterial, plant and animal cells to survive damage caused by factors of external and internal environment. Preservation HSPs response in the evolution of living matter shows that it benefits the majority of cell types. The answer HSPs is not permanent and ends after returning cells to normal conditions [16].

The importance of HSPs in the creation of proteins is reflected in the fact that the number of heat shock genes is expressed at high levels during normal cell growth. Oxygen radicals, toxins, stress and inflammatory processes improve the synthesis of HSPs and often lead to the accumulation of denatured and aberrantly folded of proteins in the cell [17, 18].

HSPs expression may be changed during glucose exhaustion and oxidative stress [19].

The metabolic pathways are activated by increasing the temperature in immunocompetent cells and lead to induction of HSPs expression. Synthesis of denatured proteins and cellular proteins is increased with amount increase of temperature. HSPs bind to newly synthesized and denatured proteins and helping their folding to the right information [20].

Heat shock proteins (HSPs) are so called because they were first observed in response to hypothermia. This is a group of binding proteins with a molecular weight of about 70 kD (the HSP

70 family). HSP 70 is present in low concentrations as molecular chaperones in unstressed cell. Concentration of HSPs is increasing rapidly in muscle of young adults during cellular stress (hypothermia, oxidative stress, exercise, changes in pH, the incorporation of new amino acids into proteins, viral infection, etc.). Increase of HSPs leads to significant changes in gene expression leading to remodeling of skeletal muscle. This response is significantly diminished in aged individuals and deficit achieved around 44% in experimental studies. Regular muscle exercise reduces decrease of HSPs [21].

It has been demonstrated that some forms of environmental stressors can induce HSPs response in fish. For example, elevated levels of various HSPs were measured in tissues of fish exposed to industrial effluents, polycyclic aromatic hydrocarbons [22], some metals such as copper, zinc and mercury [23,24] pesticides [25] and arsenic [26].

HSPs protect cells especially in lipid membranes, proteins, cytoskeletal components and nucleic acids. The protective effect applies to pathological inflammation, carcinogenesis, ischemic disorders and premature aging. There limit formation of toxic radicals and they ranked among essential quencher [16].

HSPs are involved in all important processes associated with growth, such as segmentation, DNA synthesis, transcription, translation, and protein rolling and their transport, through membranes. As an example, HSP 70, which is rolling mediator of proteins, HSP60 is chaperonin (supports post-translational accumulation of polypeptides), or HSP83, which belongs to the HSP90 proteins those genes code also chaperon proteins [22].

In stress conditions HSPs are involved of reparation of damaged proteins [9].

In relation to the immune system, HSPs significantly influence of induction and processes immune responses and HSPs are considered to be cytokines in terms of regulation of immune mechanisms. The hypothesis that the human immune system due to the strong expansion and conservation the structure of HSPs in various biological species will develop to microbial HSPs tolerance, was not confirmed. Quite the opposite, cytotoxic T Lymphocytes and specific antibodies recognize of epitopes on the microbial molecules of HSPs and indicate or directly destroy the infected cells and thus limit the infection and protect the individual. The same epitopes are also in HSPs molecules of normal cells. Risk of autoimmune reactions increases the immune response to HSPs. The simplest and most in literature described hypothesis is explaining this relationship of molecular mimikry based on homology of sequences amino acid between human and microbial HSPs [27].

HSPs were classified into several classes based on their molecular weight, such as HSP90 (85-90 kDa), HSP70 (68-73 kDa), HSP60, HSP47 and small HSPs (12-43 kDa) [28].

HSP90

Protein family HSP90 is important in the formation of steroid receptor complexes [29].

In particular, the stress protein HSP90 is a key chaperone enabling stabilized many proteins involved in malignant transformation of cells. Multiple increase of activity HSP 90 in tumor cells is an important condition for the activation of various signaling pathways sustaining cell proliferative potential and prevents apoptosis [30].

HSP70

Family HSP 70 is essential for protein synthesis, translocation and storage [31].

HSP70 can be found in different cellular compartments (nuclear, cytosolic, mitochondrial, endoplasmic reticulum, etc.) [32].

There exist many of proteins that are tied to Family HSP 70. In most species there are many proteins that appertain to Family HSP 70. Some of them are present only under stress conditions (high inductive), while some are present in cells under normal growth conditions and are not thermal inductive (constitutive or related) [32, 33].

Reduced the expression of HSP 70 may be one of the basic mechanisms participating in the development of cardiomyopathy induced by doxorubicin [34].

HSP60

Proteins of this family are also called chaperonins. They are oligomers of protein complexes. HSP60 in eukaryotes are synthesized in the cytoplasm and transported into the mitochondria. They are associated with the mitochondrial matrix and participate in saving, production and transport of proteins into mitochondria [35].

2. Conclusions

Activation heat shock protein gene (HSPs) we can consider as universal response to stress. Stress organism or cells can be induced by several factors from the outside, respectively internal environment. Among the stress factors can be included for example oxygen radicals, heavy metals, psychological stress, irradiation and inflammatory processes as well. HSPs answer is not permanent and will end after restoration of normal conditions. Genes that code the production of stress proteins in all organisms have very similar structure (for example bacteria, yeast, plants and animals) and also have a similar role. During normal cell growth was detected the number of heat shock genes at high levels. HSPs protect mainly lipid membranes, lipids, proteins, cytoskeletal components and nucleic acids in cells. HSPs are participate reparation of damaged proteins in stress conditions.

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