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Heat shock proteins and their functions

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Abstract

Heat shock proteins are a group of proteins that are observed to be produced in large amounts after cells are exposed to high temperatures. It is characterized by rapid gene expression at high temperature such as 42-46°C. These proteins are also called stress proteins because cells accept high temperature as a stress factor and synthesize heat shock proteins. There is no increase in gene expression of heat shock proteins due to high temperature alone. In addition to high temperature, there is an increase in gene expression of heat shock proteins in conditions such as UV rays, radiation, inflammation, exposure to starvation, lack of trace elements, pH change, exposure to heavy metals, and oxidative stress. The molecular weight of heat shock proteins ranges from 15 kDA to 110 kDA, and they are examined in 5 types according to their molecular weights. HSP100, HSP90, HSP70, HSP60 and (sHSP) are small heat shock proteins. Each type of HSP is located in different parts of cells and has more than one isoform. In this proceeding we will briefly discuss some of the heat shock proteins and their functions.

Introduction

Heat shock proteins are a group of proteins that were first observed to be produced in large amounts after *Drosophila Melangoster* cells were exposed to high temperatures in 1962. It is characterized by rapid gene expression at high temperature such as 42-46°C. These proteins are also called stress proteins because cells accept high temperature as a stress factor and synthesize heat shock proteins [1,2].

There is no increase in gene expression of heat shock proteins due to high temperature alone. In addition to high temperature, there is an increase in gene expression of heat shock proteins in conditions such as UV rays, radiation, inflammation, exposure to starvation, lack of trace elements, pH change, exposure to heavy metals, and oxidative stress [1,2].

The molecular weight of heat shock proteins ranges from 15 kDA to 110 kDA, and they are examined in 5 types according to their molecular weights. HSP100, HSP90, HSP70, HSP60 and (sHSP) are small heat shock proteins. Each type of HSP is located in different parts of cells and has more than one isoform [1-4].

All living things have heat shock proteins. It is one of the important protein groups that is expressed in all cell types, including prokaryotes and eukaryotes, and has managed to be preserved in the evolutionary process. It contains approximately 5% of the proteins expressed in eukaryotic cells. The strong hydrophobic interactions, hydrogen bonds and bipolar helix structure in the HSP group prevent these proteins from being denatured [1,5].

There are two factors known to be effective in the transcription of heat shock proteins. these; They are HSF1 and HSF2. In normal cells, HSF molecules are monomers and are not bound to DNA. In certain situations, for example, under stress conditions, the cell transforms into a form that has the capacity to bind HSP DNA and increase transcription to increase HSP transcription. Environmental factors in increasing transcription of HSPs

include; chemotherapeutic agents, heavy metals, inhibitory substances in energy metabolism and temperature changes are counted [1,6].

In the detection and determination of heat shock proteins; Methods such as PCR, electrophoresis, ELISA and Western blot are used [1].

Results

One of the primary functions of heat shock proteins in healthy cells, they undertake cytoprotectant functions such as correct folding of synthesized proteins and elimination of misfolded proteins, if any, folding of denatured proteins, stabilization of proteins, protein conformation, protein homeostasis, and prevention of protein aggregation. Because of these functions, they are called molecular chaperones [2].

In addition to its cytoprotectant functions, in the control of cell metabolism, regulation of cell cycle, prevention of apoptosis, mitogenesis, regulation of kinases, function of "vascular growth endotheial factor" (VGEF) receptors, which are effective in the development of many different tumors, presentation of antigens against any pathogen in the immune system, immunity It also plays a role in the cellular signal transmission pathway and intracellular substance transport [2,3].

Small Heat Shock Proteins Family (sHSP>60)

It is located in many different parts of the cell, but it is mostly seen in the cell nucleus and cytoplasm. They are usually 12-43 kDA in size. It takes part in the polymerization of protein structures such as microfilaments, microtubules and actin in the structure of the cytoskeleton. There are varieties such as HSP 16.3, HSP20, HSP25, HSP27, HSP32, HSP B9. It has effects that do not require energy use. With these effects, it prevents the agglutination of proteins. However, it maintains the continuity of other activities by interacting with HSP groups larger than itself. It acts as a chaperone, prevents cataract formation in the eye, and its mutated forms play a role in the pathogenesis of Alzheimer's and Parkinson's diseases, which are neurodegenerative diseases [1-3, 7].

The HSP60 Family

They are found in the mitochondria, cytoplasm and chloroplast of eukaryotic cells. It consists of 14 subunits. It has important roles in the realization of apoptosis, secretion of proinflammatory cytokines and insulin secretion. In addition to working alone in protein metabolism that requires energy, it also acts as a chaperone by combining with HSP10. It undertakes to provide new conformation in the folding of proteins together with HSP70. They ensure that damaged proteins are repaired without being destroyed or degraded in the cell [1-3, 7].

The HSP70 Family

It is found in the cytoplasm, nucleus, mitochondria and endoplasmic reticulum in cells. Among the heat shock protein groups, it is the protein with the most research and studies. It is available in two different forms. These; HSP72 and HSP73. It is involved in the folding of proteins, the regulation of misfolded proteins, and the control of protein activities. HSP70 is involved in more than 20% of correct protein folding [1-3, 7].

The HSP90 Family

It shows activity together with HSP100. Its best-known feature is tumorigenesis. It acts as a molecular chaperone in communication between cells, protection of morphological structures of cells, antiapoptotic pathways, regulation of steroid hormone receptors, regulation of tumor spread [1-3, 7].

The HSP100 Family

It acts as a molecular chaperone in normal cells. It is the largest family of the HSP protein group. It is also responsible for the separation of aggregating proteins, refolding and arrangement of proteins, and providing heat tolerance in plants and yeasts [1-3, 7].

Discussion

Heat shock proteins are a group of proteins that emerge under the stress condition of the cell. These stress situations occur during the formation of cancerous tissue; Self-sufficiency in cell growth, unlimited dividing ability, recovery from apoptosis with programmed cell death, invasion of tissues, and continuous angiogenesis and metastasis can be stress factors [5].

Increased HSP transcription causes suppression of these stress mechanisms. Based on this feature, it is clearly seen in the light of recent studies that it is possible to use heat shock proteins as an anticancer agent [6].

Conclusion

Future studies should focus on the utilization of the Heat shock proteins groups. For example, 17AAG, which is an inhibitor of HSP90 from heat shock proteins, not only inhibits cancerous tissues, but also increases gene expression of mutant proteins produced in cancer. Since HSP, which is used therapeutically, does not affect normal cells but only inhibits cancerous tissues, its use as a natural biological adjuvant also contributes to cancer immunotherapy studies [7].

References

1. Bener, L., Yaşar, R., & Kuran, M. (2018). Isi şok proteinleri ve in Vitro embriyo. *Black Sea Journal of Agriculture*, *1*(3), 89-93.
2. Aşkar, T. K., Ergün, N, & Turunç, V. (2007). Isı Şok Proteinler ve Fizyolojik Rolleri. Kafkas Üniversitesi Veteriner Fakültesi Dergisi, 13 (1), 109-114.
3. Öncel, M. (2012). Heat Shock Proteins and Cancer. *European Journal of Basic Medical Sciences*, *2*(1), 16-23.
4. Öztürk, E., Kahveci, N., Özlük, K., & Yılmazlar, T. (2009). Heat shock proteins. Turkish Journal of Surgery/National Journal of Surgery, 25(4), 131-136
5. Schlesinger, M. J. (1990). Heat shock proteins. *Journal of Biological Chemistry*, *265*(21), 12111-12114.
6. Tutar, L., & Tutar, Y. (2010). Heat shock proteins; an overview. *Current Pharmaceutical Biotechnology*, *11*(2), 216-222.
7. Wu, J., Liu, T., Rios, Z., Mei, Q., Lin, X., & Cao, S. (2017). Heat shock proteins and cancer. *Trends in pharmacological sciences*, *38*(3), 226-256.