



HEAT SHOCK PROTEINS (HSP)

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Introduction

Heat shock proteins (HSPs) are a family of extremely conserved proteins with a central function in plant tolerance of different types of environmental stresses, most notably heat stress. These proteins are induced at elevated temperature and other types of stresses including drought, salinity, oxidative stress, and pathogen infection. Their main function is as molecular chaperones to facilitate protein folding correction, assembly, translocation, and degradation in order to sustain cellular homeostasis. Plant HSPs are grouped into different families according to their molecular weight, for example, HSP100, HSP90, HSP70, HSP60, and sHSPs.

These are of different functions and localizations within the cell, for example, the cytosol, nucleus, mitochondria, chloroplasts, and endoplasmic reticulum. Induction of HSP is tightly controlled by heat shock transcription factor (HSF) binding to heat shock elements (HSEs) of HSP gene promoters under stress. Aside from their thermoresistance role in the classical sense, HSPs participate in developmental processes, signal transduction, and cross-tolerance to abiotic and biotic stresses. As protective agents, HSPs are now the focus of plant biotechnology for stress-resistant crop development.

Heat shock proteins are therefore a component of the plant stress response system and contribute to the adaptation and resistance of plants in fluctuating environmental conditions. Structurally equivalent but functionally different Hsps occur in the majority of organisms. A cell contains a range of Hsps in its organelles like endoplasmic reticulum, mitochondria and cytosol.

Moreover, functionally distinct but homologous Hsps are also present in the same compartment, like *S. cerevisiae* cytosol contains six distinct Hsp70 chaperones, Ssa1-4 and Ssb1-2. Certain chaperones are constitutive in the cell whereas certain other chaperones bind with different macromolecules and gain specific functions. Drugs, heat, viral, bacterial or parasitic infections, fungi, fever, inflammation, malignancy, ischemia, oxidative stresses, growth factors and hormonal stimulation induce chaperone expression. Thus, various metabolic disorders are linked with Hsps and are targets of therapy and immunization.

What are Heat Shock Proteins?

Heat shock proteins (HSPs) are a family of molecular chaperones with a specialty of assisting cells to cope with stress, especially extreme temperature, toxins, and oxidative injuries. They play a critical function of ensuring protein homeostasis by encouraging correct folding of proteins fresh from synthesis and the repair of damaged or misfolded proteins to avoid cytotoxic aggregation.

HSPs are highly conserved among all living organisms, from bacteria to human beings, testifying to their evolutionary significance. In addition to stress response, they play a role in other cellular processes such as immune responses and disease development. For example, some HSPs are involved in neurodegenerative disorders such as Alzheimer's and Parkinson's by preventing protein aggregation, whereas others are found in cancer, where they protect cancer cells from aggressive environments.

Their application in protein maintenance has been a subject of interest towards their potential use in therapy, and thus are an appropriate candidate for drug discovery in the majority of the fields of medicine. They are subfamilies based on molecular mass into various subfamilies, i.e., HSP100, HSP90, HSP70, HSP60, and small HSPs with specialized roles in cell protection and protein retention. For instance, HSP70 helps in protein folding and prevents protein aggregation, while HSP90 maintains regulatory proteins in a well-defined conformation. As protein chaperones, HSPs facilitate correct protein folding, inhibit the aggregation of misfolded proteins, and aid in protein transport and degradation to establish cellular homeostasis.

HSPs also play a crucial role in heat shock response, an evolutionarily conserved process that safeguards cells against stress in the environment. During stress conditions in cells, heat shock factors (HSFs) induce the expression of HSPs, which stabilize proteins, inhibit aggregation, and facilitate the refolding of improperly folded proteins, resulting in cell survival and function. The activities of heat shock proteins (HSPs) extend far beyond their initial characterization as hot-stress protectants. While most of the HSPs aside from ubiquitin were first described because they are heat-inducible under the state of stress, several of them are found in unstressed, normal cells in great quantities. Moreover, some of them are synthesized during specific phases of the cell cycle or development even without stress.

Hence, HSPs are enormous multi-gene superfamilies, not all of which are heat-inducible. Members of HSP families that are produced continuously, i.e., in the absence of heat stress, are referred to as HSP cognate (HSC). For the purposes of this essay, HSP cognate and HSP homolog are synonymous. We still don't know clearly how heat shock proteins (HSPs) enable organisms to survive heat. To know this, we need to learn first what each HSP does at the biochemical level.

Interestingly, studies on how the HSPs work without heat stress (under unstressed conditions) are also giving cues on how they work under stress. One of the key ideas is that HSPs keep other proteins in stable conformations and in proper folds.

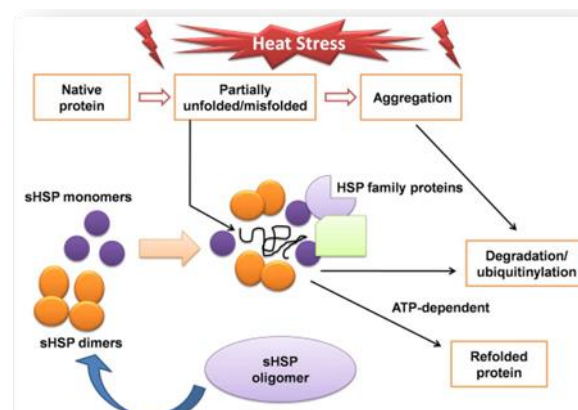


Fig 1. Mechanism of HSP Proteins

Studies prove that HSP90, HSP70, and HSP60 assist in many vital processes—folding new proteins, protein membrane transport, allowing proteins to fit in complexes, and controlling the activity of cell receptors. All these functions all include folding or repairing structure of protein chains. Due to these functions, HSP90, HSP70, and HSP60 are generally referred to as "molecular chaperones" or "polypeptide chain binding proteins." Very little has been reported regarding HSP110 in any living organism, but recent studies on a gene of the yeast HSP104—a similarly sized protein—indicate that it could be the primary function of allowing cells to survive heat.

The function of small HSPs (LMW HSPs) is not known but perhaps plays some specialized role in plants, where the protein group is highly heterogeneous. Ubiquitin, which assists in protein breakdown in cells, also takes place in heat shock, though its exact function in the process remains unknown. Overall, studies of HSPs are providing important new insights regarding plant cell behavior under stressed and unstressed conditions.

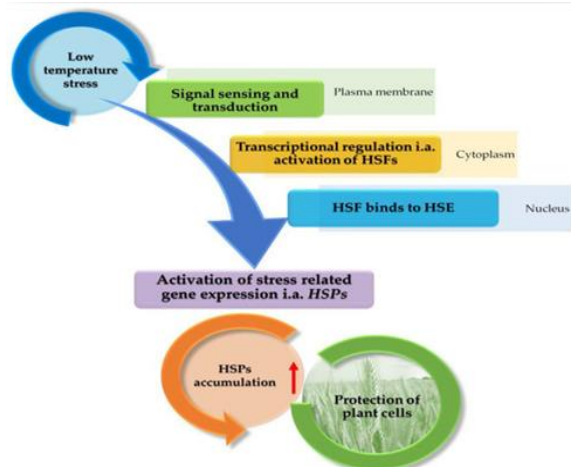


Fig 2. HSPs response to temperature stress

The heat shock response

The temperature at which the induction of the synthesis of heat shock proteins (HSPs) in organisms usually occurs is usually the range of their normal body temperatures at which each one of them naturally develops. Large HSPs are produced at all temperatures continuously in some prokaryotic genes. However, upon sudden increase in temperature or any other protein-damaging situation, expression of these genes is exceedingly quick and reaches a species-specific level within minutes. In bacteria, at the transcriptional level, heat shock response is regulated by σ^{32} polypeptide product of *rpoH* gene. Likewise, in eukaryotes, synthesis of HSP is regulated at the transcriptional level chiefly. This activity is achieved by heat shock transcription factors (HSFs) that are bound to specific DNA sequences called heat shock elements (HSEs) of HSP gene promoter sites. When a plant senses an increase in temperature, HSFs change from a monomeric state and cytoplasmic position to trimeric and nuclear. They also interact with HSEs there and stimulate the expression of HSP genes by introducing other transcriptional machinery elements to the forefront. This results in active transcription within minutes. As opposed to yeast and animals, with only a few HSFs, plants possess numerous HSF genes. For instance, tomato has more than 17 HSF genes, whereas *Arabidopsis thaliana* possesses 21. Among these, *Arabidopsis* HSF A2

is an extremely important regulator of environmental stress responses. One of the most typical features of thermotolerance is resistance to heat in gene expression.

Heat stress triggers a sudden change in the pattern of gene expression by inducing the synthesis of heat shock proteins (Hsps) and inhibiting expression of most of the genes expressed at non-stress temperature. Non-heat stress response protein mRNAs are destabilized during heat stress. Splicing reactions are also inhibited, and it is believed that Hsp-coding mRNAs are properly processed since the genes that encode Hsps do not have introns in general. Heat shock response also involves a tremendous reorganization of proteins in cells. These redistributions are both on the microscale and the macroscale. On the microscale, these involve RNA polymerase II (RNAPII) release from constitutive housekeeping genes to the heat shock-activated genes and attachment of activated nuclear heat shock promoter regions to cytoplasmic heat shock transcription factors. On the cellular level, there are many reorganizations of larger significance that take place following heat stress. These include cytoskeleton modification, histone protein assembly into chromatin, and heat shock granule assembly (HSGs). Return to normal distribution of proteins is crucial in the recovery process. Recovery is more effective in thermotolerant cells and must happen for the recovery of normal cell function.

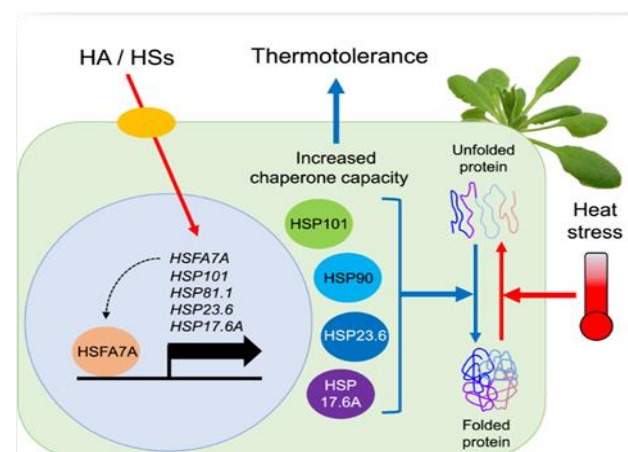


Fig 3. HSPs response to heat stress

Conclusion

The most important among the reasons for plant loss globally are abiotic stresses, particularly temperature stresses, salinity, and drought. In addition to these, plants are also repeatedly exposed to severe day-to-day and season-to-season variations of temperature and need to acclimatize continuously toward moving environmental regimes and genetic stresses on a daily basis. Heat shock proteins (Hsps) are involved in the protection against environmental variation and therefore in homeostasis during the changing environment. Hsps constitute a vital nexus in increasing resistance to stress and facilitating plant adaptation to environmental stress. Greater understanding of their function in stress tolerance—i.e., applied—may allow them to be effective markers of plant stress.

The genes coding Hsps have been investigated more intensively due to technology. Integrated technologies involving genomics techniques such as quantitative trait loci (QTL) mapping, microarray, and quantitative PCR being integrated with proteomics techniques such as 2-D gel electrophoresis, X-ray crystallography, and nuclear magnetic resonance (NMR) spectroscopy are shedding light on the stress effect at the DNA, RNA, and protein levels. Coupled with conventional protein expression analysis techniques, such technology is uncovering the expression and regulation of heat shock proteins ever greater depth of detail.

References

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