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Review

Heat shock response in photosynthetic organisms: Membrane and lipid connections

Ibolya Horváth [a], Attila Glatz [a], Hitoshi Nakamoto [b,c], Michael L. Mishkind [d], Teun Munnik [e], Yonousse Saidi [f], Pierre Goloubinoff [f], John L. Harwood [g,*], László Vigh [a,*]

[a] Institute of Biochemistry, Biol. Res. Centre, Hungarian Acad. Sci., Temesvári krt. 62, H-6734 Szeged, Hungary
[b] Department of Biochemistry and Molecular Biology, Saitama University, Saitama 338-8570, Japan
[c] Institute for Environmental Science and Technology (IEST), Saitama University, Saitama 338-8570, Japan
[d] National Science Foundation, Division of Integrative Organismal Systems, 4201 Wilson Boulevard, Arlington, VA 22230, USA
[e] Section of Plant Physiology, Swammerdam Institute for Life Science, University of Amsterdam, Science Park 904, 098 XH, Amsterdam, The Netherlands
[f] Department of Plant Molecular Biology, Faculty of Biology and Medicine, University of Lausanne, Lausanne, Switzerland
[g] School of Biosciences, Cardiff University, Cardiff CF10 3AF, Wales, UK

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ABSTRACT

The ability of photosynthetic organisms to adapt to increases in environmental temperatures is becoming more important with climate change. Heat stress is known to induce heat-shock proteins (HSPs) many of which act as chaperones. Traditionally, it has been thought that protein denaturation acts as a trigger for HSP induction. However, increasing evidence has shown that many stress events cause HSP induction without commensurate protein denaturation. This has led to the membrane sensor hypothesis where the membrane's physical and structural properties play an initiating role in the heat shock response.

In this review, we discuss heat-induced modulation of the membrane's physical state and changes to these properties which can be brought about by interaction with HSPs. Heat stress also leads to changes in lipid-based signaling cascades and alterations in calcium transport and availability. Such observations emphasize the importance of membranes and their lipids in the heat shock response and provide a new perspective for guiding further studies into the mechanisms that mediate cellular and organismal responses to heat stress.

Contents

Abbreviations: BA, benzyl alcohol; DAG, diacylglycerol; DPI, diphenylene iodonium; HSP, heat-shock protein; HSR, heat-shock response; IP_3, inositol-1,4,5-trisphosphate; IP_6, inositol hexaphosphate (phytic acid); JDP, J-domain protein; NBD, nucleotide binding domain; MD, middle domain; MG1cDG, monoglucosyl-diacylglycerol; NEF, nucleotide exchange factor; PA, phosphatidic acid; PIP_2, Phosphatidylinositol 4, 5-bisphosphate; PIPK, phosphatidylinositol 4-phosphate kinase; PLC, phospholipase C; PLD, phospholipase D; sHSP, small heat-shock protein (generally less than 45 kDa).

* Corresponding authors. Tel.: +44 2920 874108; fax: +44 2920 874116 (J.L. Harwood), tel./fax: +36 62 432048 (L. Vigh).
E-mail addresses: Harwood@cardiff.ac.uk (J.L. Harwood), Vigh@brc.hu (L. Vigh).

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1. Introduction

Temperature is continually changing within the environment, both during the day and with the season. Photosynthetic organisms, such as plants and cyanobacteria are directly exposed to acute temperature alterations as well as climate change. Photosynthesis is considered among the most heat sensitive cell functions and, among its various components, the oxygen-evolving complex of photosystem II (PSII) is the most heat sensitive [1]. A mild sublethal temperature stress causes the rapid reprogramming of cellular activity to ensure survival during a subsequent exposure to noxious heat stress. This phenomenon called *acquired thermotolerance* depends on a prior priming mild heat treatment which is essential to induce the timely accumulation of cell components that reduce heat damage and mediate a rapid recovery of the cellular function during a subsequent recovery period. Many data indicate that, following a sub-lethal priming mild heat stress, there is an induction of heat-shock proteins (HSPs) that correlates with the development of acquired thermotolerance.

Here we briefly mention five highly-conserved ubiquitously distributed HSP-families – all molecular chaperones – that are responsible in a major way for the onset of thermotolerance in plants. We then consider these results in the context of the growing appreciation that membrane lipids also play key roles in the acclimation of plants and cyanobacteria to stressful high temperatures.

The early demonstration that formation in heat-stressed cells of damaged, non-native proteins alone is necessary and sufficient to activate hsp genes provided a conceptual framework for the view that HSPs (like, HSP90 and HSP70) may become recruited by heat-denatured proteins thereby acting as part of a "cellular thermometer" [3]. But several lines of evidence suggest that high temperature, cold and osmotic stress might be perceived by plants and cyanobacteria also via changes in the fluidity of their cell membranes [4–7]. It has been suggested that the elevation of membrane fluidity caused by the increased temperatures can activate the expression of hsp genes. Evidence to support this concept for photosynthetic cells was obtained first in *Synechocystis* PCC6803 [5]. At non-heat-shock temperatures, the membrane fluidizer benzyl alcohol (BA) activated the transcription of some hsp genes apparently as efficiently as heat stress. The "membrane sensor" hypothesis outlined here is by no means exclusive. Besides thermally-induced changes in membrane organization and protein conformation, the hypothetical list of possible thermometers includes alteration of RNA and histones as suggested recently [8]. Nevertheless, the central dogma in this field has been that the primary heat shock signal occurs as a feedback reaction to the accumulation of damaged proteins. Another possibility, which intuitively appears more appropriate for cell homeostasis under non-damaging mild warming conditions, is that a signal is generated *before* any damage has occurred: mild heat causing small incremental changes in membrane fluidity would be perfectly optimally capable of alerting the cell to an upcoming noxious heat stress in order to generate a timely molecular response of defense.

Upon exposure to heat, a subset of HSPs, in particular the small HSPs (sHSP) become membrane-associated, localizing within specific membrane domains, thereby correcting in part the lipid order and phase-state of the membranes [9]. As also discussed below, such crosstalk between the primary heat-sensor, the membranes and the HSPs indicate a possible feedback mechanism to regulate their gene expression.

Heat shock, like many other stresses, induces specific and highly-regulated signaling cascades leading to the transcriptional up-regulation of hsp genes. Here, we present new data on the operation of heat shock-activated phospholipid-based sensing and signaling pathways. It is suggested that in plants, a small G-protein coordinates the activity of phosphatidylinositol (4)-phosphate kinase (PIPK) and phospholipase D (PLD) during the response to heat stress, responsible for the accumulation of the two key signaling lipids, phosphatidylinositol (4,5)-bisphosphate (PIP_2) and phosphatidic acid (PA).

Finally, in support of a central heat-sensing role of membranes, we will discuss recent experimental evidence that both heat and chemical manipulation of membrane fluidity can trigger a specific, transient Ca^{2+} influx from outside of the cell. Calcium entry across the plasma membrane is essential for heat to induce hsp genes. Remarkably, membrane fluidizers also activate hsp genes at constant low temperature in a strict calcium-dependent manner [6]. Taken together, these data suggest that early sensing of mild temperature increases occurs at the plasma membrane of plant cells independently from cytosolic protein unfolding.

2. Plant and cyanobacterial heat shock proteins

Higher plant genomes contain about 300 genes encoding for molecular chaperones, co-chaperones and foldases. Whereas a non-lethal heat shock in Arabidopsis can up-regulate about 1300 genes, only 90 of them belong to the highly conserved families of molecular chaperones. The other 210 chaperones, co-chaperones and foldases which are not induced by heat and therefore cannot be called HSPs, may instead be induced by other stresses or are developmentally expressed in specific organs or remain constitutively expressed to carry out house keeping functions in protein homeostasis [2]. Thus, molecular chaperones take part both in many physiological as well as stress-related cellular processes. Ample evidence from transgenic plants has shown that HSP-chaperones are important for plant development and response to various stresses. All the five representative HSPs (below) are members of highly-conserved ubiquitously-distributed protein families. They are classified on the basis of their sequence similarity and named according to their approximate molecular masses on SDS