

Indu

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Keith

Journal of Biological Chemistry

Aha1 Can Act as an Autonomous Chaperone to Prevent Aggregation of Stressed Proteins

December 26, 2014 The Journal of Biological Chemistry, 289, 36220-36228.

Vishwadeepak Tripathi, Stefanie Darnauer, Nadine R. Hartwig and Wolfgang M. J. Obermann¹

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Aha1 (activator of Hsp90 ATPase) stimulates the ATPase activity of the molecular

chaperone Hsp90 to accelerate the conformational cycle during which client proteins attain their final shape. Thereby, Aha1 promotes effective folding of Hsp90-dependent clients such as steroid receptors and many kinases involved in cellular signaling. In our current study, we find that Aha1 plays a novel, additional role beyond regulating the Hsp90 ATP hydrolysis rate. We propose a new concept suggesting that Aha1 acts as an autonomous chaperone and associates with stress-denatured proteins to prevent them from aggregation similar to the chaperonin GroEL. Our study reveals that an N-terminal sequence of 22 amino acids, present in human but absent from yeast Aha1, is critical for this capability. However, in lieu of fostering their refolding, Aha1 allows ubiquitination of bound clients by the E3 ubiquitin ligase CHIP. Accordingly, Aha1 may promote disposal of folding defective proteins by the cellular protein quality control.

Unfolded Protein Response-regulated *Drosophila* Fic (dFic) Protein Reversibly AMPylates BiP Chaperone during Endoplasmic Reticulum Homeostasis

December 26, 2014 The Journal of Biological Chemistry, 289, 36059-36069.

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Drosophila Fic (dFic) mediates AMPylation, a covalent attachment of adenosine monophosphate (AMP) from ATP to hydroxyl side chains of protein substrates. Here, we identified the endoplasmic reticulum (ER) chaperone BiP as a substrate for dFic and mapped the modification site to Thr-366 within the ATPase domain. The level of AMPylated BiP in *Drosophila* S2 cells is high during homeostasis, whereas the level of AMPylated BiP decreases upon the accumulation of misfolded proteins in the ER. Both dFic and BiP are transcriptionally activated upon ER stress, supporting the role of dFic in the unfolded protein response pathway. The inactive conformation of BiP is the preferred substrate for dFic, thus endorsing a model whereby AMPylation regulates the function of BiP as a chaperone, allowing acute activation of BiP by deAMPylation during an ER stress response. These findings not only present the first substrate of eukaryotic AMPylator but also provide a target for regulating the unfolded protein response, an emerging avenue for cancer therapy.

Nathen

Proteogenomic analysis and global discovery of posttranslational modifications in prokaryotes

Ming-kun Yanga, Yao-hua Yanga, Zhuo Chena, Jia Zhanga, Yan Lina, Yan Wang, Qian Xiong, Tao Lia, Feng Gea, Donald A. Bryantb, and Jin-dong Zhaoa

We describe an integrated workflow for proteogenomic analysis and global profiling of posttranslational modifications (PTMs) in prokaryotes and use the model cyanobacterium *Synechococcus* sp. PCC 7002 (hereafter *Synechococcus* 7002) as a test case. We found more than 20 different kinds of PTMs, and a holistic view of PTM events in this organism grown under different conditions was obtained without specific enrichment strategies. Among 3,186 predicted protein-coding genes, 2,938 gene products (>92%) were identified. We also identified 118 previously unidentified proteins and corrected 38 predicted gene-coding regions in the *Synechococcus* 7002 genome. This systematic analysis not only provides comprehensive information on protein profiles and the diversity of PTMs in *Synechococcus* 7002 but also provides some insights into photosynthetic pathways in cyanobacteria. The entire proteogenomics pipeline is applicable to any sequenced prokaryotic organism, and we suggest that it should become a standard part of genome annotation projects

Functions of Heat Shock Proteins in Pathways of the Innate and Adaptive Immune System

Robert Julian Binder

For more than 50 years, heat shock proteins (HSPs) have been studied for their role in protecting cells from elevated temperature and other forms of stress. More recently, several roles have been ascribed to HSPs in the immune system. These include intracellular roles in Ag presentation and expression of innate receptors, as well as extracellular roles in tumor immunosurveillance and autoimmunity. Exogenously administered HSPs can elicit a variety of immune responses that have been used in immunotherapy of cancer, infectious diseases, and autoimmune disease.

Minsoo

. Cell Rep. 2015 Jan 6;10(1):47-61. doi: 10.1016/j.celrep.2014.12.006. Epub 2014 Dec 24.

Dicer and hsp104 function in a negative feedback loop to confer robustness to environmental stress.

Oberti D(1), Biasini A(1), Kirschmann MA(1), Genoud C(1), Stunnenberg R(1), Shimada Y(1), Bühler M(2).

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Epigenetic mechanisms can be influenced by environmental cues and thus evoke phenotypic variation. This plasticity can be advantageous for adaptation but also detrimental if not tightly controlled. Although having attracted considerable interest, it remains largely unknown if and how environmental cues such as temperature trigger epigenetic alterations. Using fission yeast, we demonstrate that environmentally induced discontinuous phenotypic variation is buffered by a negative feedback loop that involves the RNase Dicer and the protein disaggregase Hsp104. In the absence of Hsp104, Dicer accumulates in cytoplasmic inclusions and heterochromatin becomes unstable at elevated temperatures, an epigenetic state inherited for many cell divisions after the heat stress. Loss of Dicer leads to toxic aggregation of an exogenous prionogenic protein. Our results highlight the importance of feedback regulation in building epigenetic memory and uncover Hsp104 and Dicer as homeostatic controllers that buffer environmentally induced stochastic epigenetic variation and toxic aggregation of prionogenic proteins.

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Dan

Overexpression of heat stress-responsive *TaMBF1c*, a wheat (*Triticum aestivum* L.) Multiprotein Bridging Factor, confers heat tolerance in both yeast and rice

Abstract:

Previously, we found an ethylene-responsive transcriptional co-activator, which was significantly induced by heat stress (HS) in both thermo-sensitive and thermo-tolerant wheat. The corresponding ORF was isolated from wheat, and named *TaMBF1c* (*Multiprotein Bridging Factor1c*). The deduced amino acid sequence revealed the presence of conserved MBF1 and helix-turn-helix domains at the N- and C-terminus, respectively, which were highly similar to rice ERTCA (Ethylene Response Transcriptional Co-Activator) and *Arabidopsis* MBF1c. The promoter region of *TaMBF1c* contained three heat shock elements (HSEs) and other stress-responsive elements. There was no detectable mRNA of *TaMBF1c* under control conditions, but the transcript was rapidly and significantly induced by heat stress not only at the seedling stage, but also at the flowering stage. It was also slightly induced by drought and H₂O₂ stresses, as well as by application of the ethylene synthesis precursor ACC, but not, however, by circadian rhythm, salt, ABA

or MeJA treatments. Under normal temperatures, TaMBF1c-eGFP protein showed predominant nuclear localization with some levels of cytosol localization in the bombarded onion epidermal cells, but it was mainly detected in the nucleus with almost no eGFP signals in cytosol when the bombarded onion cells were cultured under high temperature conditions. Overexpression of *TaMBF1c* in yeast imparted tolerance to heat stress compared to cells expressing the vector alone. Most importantly, transgenic rice plants engineered to overexpress *TaMBF1c* showed higher thermotolerance than control plants at both seedling and reproductive stages. In addition, transcript levels of six [Heat Shock Protein](#) and two Trehalose Phosphate Synthase genes were higher in *TaMBF1c* transgenic lines than in wild-type rice upon heat treatment. Collectively, the present data suggest that *TaMBF1c* plays a pivotal role in plant thermotolerance and holds promising possibilities for improving heat tolerance in crops.

Damian

Cell

Christopher Hine, Eylul Harputlugil, Yue Zhang, Christoph Ruckenstuhl, Byung Cheon Lee, Lear Brace, Alban Longchamp, Jose H. Treviño-Villarreal, Pedro Mejia, C. Keith Ozaki, Rui Wang, Vadim N. Gladyshev, Frank Madeo, William B. Mair, James R. Mitchell,

Endogenous Hydrogen Sulfide Production Is Essential for Dietary Restriction Benefits,

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Dual Proteolytic Pathways Govern Glycolysis and Immune Competence,

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Tomoyuki Mashimo, Kumar Pichumani, Vamsidhara Vemireddy, Kimmo J. Hatanpaa, Dinesh Kumar Singh, Shyam Sirasanagandla, Suraj Nannepaga, Sara G. Piccirillo, Zoltan Kovacs, Chan Foong, Zhiguang Huang, Samuel Barnett, Bruce E. Mickey, Ralph J. DeBerardinis, Benjamin P. Tu, Elizabeth A. Maher, Robert M. Bachoo, Acetate Is a Bioenergetic Substrate for Human Glioblastoma and Brain Metastases, Cell, Volume 159, Issue 7, 18 December 2014, Pages 1603-1614, ISSN 0092-8674, <http://dx.doi.org/10.1016/j.cell.2014.11.025>.

Plant Journal

The response of *Chlamydomonas reinhardtii* to nitrogen deprivation: A systems biology analysis

Jeong-Jin Park, Hongxia Wang, Mahmoud Gargouri, Rahul Deshpande, Jeremy N. Skepper, F. Omar Holguin, Matthew Juergens, Yair Shachar-Hill, Leslie M. Hicks and David R. Gang

Accepted manuscript online: 17 DEC 2014 02:19AM EST | DOI: 10.1111/tpj.12747

THB1, a truncated haemoglobin, modulates nitric oxide levels and nitrate reductase activity

Emanuel Sanz-Luque, Francisco Ocaña-Calahorro, Amaury de Montaigu, Alejandro Chamizo-Ampudia, Ángel Llamas, Aurora Galván and Emilio Fernández

Accepted manuscript online: 11 DEC 2014 08:46AM EST | DOI: 10.1111/tpj.12744

Modelling central metabolic fluxes by constraint-based optimization reveals metabolic reprogramming of developing *Solanum lycopersicum* (tomato) fruit(pages 24–39)

Sophie Colombié, Christine Nazaret, Camille Bénard, Benoît Biais, Virginie Mengin, Marion Solé, Laëtitia Fouillen, Martine Dieuaide-Noubhani, Jean-Pierre Mazat, Bertrand Beauvoit and Yves Gibon

Plant Physiology

- Chunyang Wang,
- Yang Liu,
- Si-Shen Li,
- and Guan-Zhu Han

Insights into the origin and evolution of plant hormone signaling machinery

Plant Physiol. pp.114.247403; First Published on January 5, 2015;doi:10.1104/pp.114.247403

- Chao Wu,
- Wei Xiong,
- Junbiao Dai,

· and Qingyu Wu

Genome-based Metabolic Mapping and ¹³C Flux Analysis Reveal Systematic Properties of an Oleaginous Microalga *Chlorella protothecoides*

Plant Physiol. pp.114.250688; First Published on December 15, 2014;doi:10.1104/pp.114.250688

· Nak Hyun Kim and

· Byung Kook Hwang

Pepper Heat Shock Protein 70a Interacts with the Type III Effector AvrBsT and Triggers Plant Cell Death and Immunity

Plant Physiol. pp.114.253898; First Published on December 9, 2014;doi:10.1104/pp.114.253898

Fionn

[J Biol Chem](#). 2014 Dec 18.

[Kalderon B](#)¹, [Kogan G](#)¹, [Bubis E](#)¹, [Pines O](#)².

Cytosolic Hsp60 can modulate proteasome activity in yeast.

Abstract

Hsp60, an essential oligomeric molecular mitochondrial chaperone, has been subject to rigorous basic and clinical research. With yeast as a model system, we provide evidence for the ability of cytosolic yHsp60 to inhibit the yeast proteasome: i) Following biological turnover of Murine-Bax (aproteasome substrate), we show that co-expression of cytosolic yHsp60 stabilizes Bax, enhances its association with mitochondria and enhances its killing capacity. ii) Expression of yHsp60 in the yeast cytosol (yHsp60c) inhibits degradation of a cytosolic protein Δ MTS-Aco1 tagged with the degron SL17 (a ubiquitin-proteasome substrate). iii) Conditions under which Hsp60 accumulates in the cytosol (elevated Hsp60c or growth at 37°C) correlate with reduced 20S peptidase activity in proteasomes purified from cell extracts. iv) Elevated yHsp60 in the cytosol correlate with accumulation of poly-ubiquitinated proteins. v) According to 20S proteasome pull down experiments, Hsp60 is physically associated with proteasomes in extracts of cells expressing Hsp60c or grown at 37°C. Even mutant Hsp60 proteins, lacking chaperone activity, were still capable of proteasome inhibition. The results support the hypothesis, that localization of Hsp60 to the cytosol may modulate proteasome activity according to cell need.

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