

Damian:

Plant Journal August 1st 2013 (pages 377–389)

An Arabidopsis homolog of importin β 1 is required for ABA response and drought tolerance
Yanjie Luo, Zhijuan Wang, Hongtao Ji, Hui Fang, Shuangfeng Wang, Lining Tian and Xia Li

The import of proteins into the nucleus in response to drought is critical for mediating the reprogramming of gene expression that leads to drought tolerance. However, regulatory mechanisms involved in nuclear protein import remain largely unknown. Here, we have identified an Arabidopsis gene (*AtKPNB1*) as a homolog of human *KPNB1* (importin β 1). *AtKPNB1* was expressed in multiple organs, and the protein was localized in the cytoplasm and nucleus. *AtKPNB1* was able to facilitate nuclear import of a model protein. Null mutation of *AtKPNB1* delayed development under normal growth conditions and increased sensitivity to abscisic acid (ABA) during seed germination and cotyledon development. Inactivation of *AtKPNB1* increased stomatal closure in response to ABA, reduced the rate of water loss, and substantially enhanced drought tolerance. *AtKPNB1* interacted with several importin α proteins, nucleoporin AtNUP62, and the Arabidopsis Ran proteins. Inactivation of *AtKPNB1* did not affect the ABA responsiveness or the expression level or subcellular localization of ABI1, ABI2 or ABI5, key regulators of the ABA signaling pathway. Moreover, phenotypic analysis of epistasis revealed that *AtKPNB1* modulates the ABA response and drought tolerance through a pathway that is independent of ABI1 and ABI5. Collectively, our results show that *AtKPNB1* is an Arabidopsis importin β that functions in ABA signaling.

In one sentence: The Arabidopsis homolog of nuclear importin KPNB1 is a negative regulator of drought tolerance and ABA-dependent responses.

Background: Drought tolerance in plants is mediated by ABA-dependent and ABA-independent pathways. ABA-dependent pathway involves ABA binding to PYR/PYL proteins, which leads to binding and inhibition of ABI1/2, thus allowing for phosphorylation of SnRKs. Fionn, of course, can tell you about those. This ultimately culminates in things like germination delay, dormancy, stomatal closure. I'll add that ROS, including H₂O₂ and NO, have been implicated in this signal transduction cascade. Anyway, this group mentions, seemingly without provocation, that translocation of proteins in and out of the nucleus is critical to this process, and that mutation in an Arabidopsis homolog of a human Ran protein leads to ABA hyper-responsiveness. So just a little review, I know I need it, I'm not exactly a nuclear trafficking expert—proteins enter the nucleus via NLSs (stretch of basic amino acids—NLS is bound by importin alpha, which binds importin beta, which binds to the nuclear pore complex, which—after opening up and letting the complex into the nucleoplasm—coordinates with a Ran GTPase, which binds importin beta and causes complex dissociation. So, why do we care? Because when the authors of this paper carried out a screen for differences in drought sensitivity among TDNA mutants in importin beta genes, they turned up an importin beta whose mutation led to improved drought tolerance. They mention one importin beta came out of the screen. There are actually 17 importin beta genes in Arabidopsis. So, I guess this is the one that panned out? Perhaps others also show ABA responses too, but the authors do not mention them.

Results: KPNB1 mutants exhibited less water loss, smaller stomatal apertures upon ABA treatment, and higher plant survival rates upon drought treatment, as well as greater tolerance to osmotic stress (both ionic NaCl and non-ionic mannitol). Also, growth was slower, germination was delayed (and hypersensitive to ABA), and plants were semi-dwarf at flowering. All of these were complemented with an over-expression transgene. Chalcone synthase with an NLS-GFP tag accumulated less in the nucleus of *kpnb1* null plants. KPNB1 interacts with two of nine importin alpha, one nucleoporin, and three of four Ran-GTP proteins in Y2H and BiFC. Transcripts of ABA-activated genes (downstream of ABI5) were higher in the *kpnb1* plants than Col-0, whereas *ABI3/5* transcripts looked pretty damn similar in mutant and wild-type. Loss of function mutations in *ABI1*

and *ABI5* led to worsening and abating of the phenotypes, respectively. However, neither of these proteins appeared to localize differently (nucleus vs. cytosol) in the *kpnb* background.

Significance: KPNB1 is a nuclear importin beta that probably helps to import proteins that negatively regulate ABA-dependent drought tolerance, germination inhibition, etc. But which proteins are these? Apparently chalcone synthase was affected, but not ABI1 or ABI5. I wonder if there are other nuclear importins whose knockout causes the opposite—ABA insensitivity and drought sensitivity?

Cell July 18th 2013 page 365

Noncanonical Autophagy Promotes the Visual Cycle

Ji-Young Kim, Hui Zhao, Jennifer Martinez, Teresa Ann Doggett, Alexander V. Kolesnikov, Peter H. Tang, Zsolt Ablonczy, Chi-Chao Chan, Zhenqing Zhou, Douglas R. Green, Thomas A. Ferguson

Phagocytosis and degradation of photoreceptor outer segments (POS) by retinal pigment epithelium (RPE) is fundamental to vision. Autophagy is also responsible for bulk degradation of cellular components, but its role in POS degradation is not well understood. We report that the morning burst of RPE phagocytosis coincided with the enzymatic conversion of autophagy protein LC3 to its lipidated form. LC3 associated with single-membrane phagosomes containing engulfed POS in an Atg5-dependent manner that required Beclin1, but not the autophagy preinitiation complex. The importance of this process was verified in mice with Atg5-deficient RPE cells that showed evidence of disrupted lysosomal processing. These mice also exhibited decreased photoreceptor responses to light stimuli and decreased chromophore levels that were restored with exogenous retinoid supplementation. These results establish that the interplay of phagocytosis and autophagy within the RPE is required for both POS degradation and the maintenance of retinoid levels to support vision.

In one sentence: This group shows that phagocytosis of photoreceptors' outer segments (OS) is a form of autophagy.

Background: Vision depends on a G-protein coupled receptor (opsin) that changes conformation in response to visual stimulation, caused by the isomerization of 11-cis retinal to all-trans retinal. These processes occur in the outer segment of photoreceptor cells (rods and cones), outer segments being extensions of lamellar endomembranes derived from the plasmalemma and comprising the majority of the cell volume in the structure of an oblong cilium. Photoreceptor cells are intuitively prone to oxidative damage, so the outer segment lamella have to be turned over frequently. To wit, the most-outer of the outer segment is exocytosed, and this exocytic vesicle is phagocytosed by retinal epithelial cells.

Results: Using mice, deletion of retinal epithelium ATG5 (an autophagy protein) disrupts visual function, but does not result in a change in the number of rods or cones. The autophagy proteins ATG5 and LC3 were found to localize to the membranes of outer segment (OS) phagosomes— intriguing, given that autophagosomes tend to be double-membraned. Silencing of autophagy proteins always disrupted general autophagy, but did not always interfere with OS phagocytosis/turnover, indicating that a subset of autophagy proteins are necessary for OS turnover, but not all of them. And in all cases, OS was engulfed, even if not turned over, indicating that the endocytosis itself doesn't require autophagy to proceed. Vitamin A metabolites were similar between mutants and controls, but active and post-active 11-cis and all-trans retinal were much lower. Injection of 11-cis into the blood led to a short-term recovery of visual function in the mutants.

Significance: If OS turnover is disrupted, photoreceptors are like perfectly good engines with no fuel in them. Chromophore recycling, as well as organellar development, requires a specialized form of autophagy.

Indu

1. Science. 2013 Jul 19;341(6143):1238303. doi: 10.1126/science.1238303.

Tight coordination of protein translation and HSF1 activation supports the anabolic malignant state.

Santagata S, Mendillo ML, Tang YC, Subramanian A, Perley CC, Roche SP, Wong B, Narayan R, Kwon H, Koeva M, Amon A, Golub TR, Porco JA Jr, Whitesell L, Lindquist S.

Department of Pathology, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA 02215, USA.

Comment in

Science. 2013 Jul 19;341(6143):242-3.

The ribosome is centrally situated to sense metabolic states, but whether its activity, in turn, coherently rewire transcriptional responses is unknown. Here, through integrated chemical-genetic analyses, we found that a dominant transcriptional effect of blocking protein translation in cancer cells was

inactivation of heat shock factor 1 (HSF1), a multifaceted transcriptional regulator of the heat-shock response and many other cellular processes essential for anabolic metabolism, cellular proliferation, and tumorigenesis. These analyses linked translational flux to the regulation of HSF1 transcriptional activity and to the modulation of energy metabolism. Targeting this link with translation initiation inhibitors such as rocaglates deprived cancer cells of their energy and chaperone armamentarium and selectively impaired the proliferation of both malignant and premalignant cells with early-stage oncogenic lesions.

Stephanie:

[Plant Mol Biol.](#)

Cochaperonin CPN20 negatively regulates abscisic acid signaling in Arabidopsis.

[Zhang XF](#), [Jiang T](#), [Wu Z](#), [Du SY](#), [Yu YT](#), [Jiang SC](#), [Lu K](#), [Feng XJ](#), [Wang XF](#), [Zhang DP](#).

Source

MOE Systems Biology and Bioinformatics Laboratory, School of Life Sciences, Tsinghua University, Beijing, 100084, China.

Abstract

Previous study showed that the magnesium-protoporphyrin IX chelatase H subunit (CHLH/ABAR) positively regulates abscisic acid (ABA) signaling. Here, we investigated the functions of a CHLH/ABAR interaction protein, the chloroplast co-chaperonin 20 (CPN20) in ABA signaling in *Arabidopsis thaliana*. We showed that down-expression of the CPN20 gene increases, but overexpression of the CPN20 gene reduces, ABA sensitivity in the major ABA responses including ABA-induced seed germination inhibition, postgermination growth arrest, promotion of stomatal closure and inhibition of stomatal opening. Genetic evidence supports that CPN20 functions

downstream or at the same node of CHLH/ABAR, but upstream of the WRKY40 transcription factor. The other CPN20 interaction partners CPN10 and CPN60 are not involved in ABA signaling. Our findings show that CPN20 functions negatively in the ABAR-WRKY40 coupled ABA signaling independently of its co-chaperonin role, and provide a new insight into the role of co-chaperones in the regulation of plant responses to environmental cues.

Yichen:

J Mol Biol. 2013 Aug 23;425(16):2922-39. doi: 10.1016/j.jmb.2013.05.019. Epub 2013 May 29.

Chaperone-Interacting TPR Proteins in *Caenorhabditis elegans*.

Haslbeck V, Eckl JM, Kaiser CJ, Papsdorf K, Hessling M, Richter K.

Source

Center for Integrated Protein Science Munich and Department of Chemistry, Technische Universität München, 85747 Garching, Germany.

Abstract

The ATP-hydrolyzing molecular chaperones Hsc70/Hsp70 and Hsp90 bind a diverse set of tetratricopeptide repeat (TPR)-containing cofactors via their C-terminal peptide motifs IEEVD and MEEVD. These cochaperones contribute to substrate turnover and confer specific activities to the chaperones. Higher eukaryotic genomes encode a large number of TPR-domain-containing proteins. The human proteome contains more than 200 TPR proteins, and that of *Caenorhabditis elegans*, about 80. It is unknown how many of them interact with Hsc70 or Hsp90. We systematically screened the *C. elegans* proteome for TPR-domain-containing proteins that likely interact with Hsc70 and Hsp90 and ranked them due to their similarity with known chaperone-interacting TPRs. We find *C. elegans* to encode many TPR proteins, which are not present in yeast. All of these have homologs in fruit fly or humans. Highly ranking uncharacterized open reading frames C33H5.8, C34B2.5 and ZK370.8 may encode weakly conserved homologs of the human proteins RPAP3, TTC1 and TOM70. C34B2.5 and ZK370.8 bind both Hsc70 and Hsp90 with low micromolar affinities. Mutation of amino acids involved in EEVD binding disrupts the interaction. In vivo, ZK370.8 is localized to mitochondria in tissues with known chaperone requirements, while C34B2.5 colocalizes with Hsc70 in intestinal cells. The highest-ranking open reading frame with non-conserved EEVD-interacting residues, F52H3.5, did not show any binding to Hsc70 or Hsp90, suggesting that only about 15 of the TPR-domain-containing proteins in *C. elegans* interact with chaperones, while the many others may have evolved to bind other ligands.

Fionn:

Nature

Three-state mechanism couples ligand and temperature sensing in riboswitches

Anke Reining, Senada Nozinovic, Kai Schlepckow, Florian Buhr, Boris Fürtig & Harald Schwalbe

Riboswitches are *cis*-acting gene-regulatory RNA elements that can function at the level of transcription, translation and RNA cleavage^{1, 2, 3}. The commonly accepted molecular mechanism for riboswitch function proposes a ligand-dependent conformational switch between two mutually exclusive states⁴. According to this mechanism, ligand binding to an aptamer domain induces an allosteric conformational switch of an expression platform, leading to activation or repression of ligand-related gene expression⁵. However, many riboswitch properties cannot be explained by a pure two-state mechanism. Here we show that the regulation mechanism of the adenine-sensing riboswitch, encoded by the *add* gene on chromosome II of the human Gram-negative pathogenic bacterium *Vibrio vulnificus*⁶, is notably different from a two-state switch mechanism in that it involves three distinct stable conformations. We characterized the temperature and Mg²⁺ dependence of the population ratios of the three conformations and the kinetics of their interconversion at nucleotide resolution. The observed temperature dependence of a pre-equilibrium involving two structurally distinct ligand-free conformations of the *add* riboswitch conferred efficient regulation over a physiologically relevant temperature range. Such robust switching is a key requirement for gene regulation in bacteria that have to adapt to environments with varying temperatures. The translational adenine-sensing riboswitch represents the first example, to our knowledge, of a temperature-compensated regulatory RNA element.

China needs workers more than academics

Nature biotech

Chaperones as thermodynamic sensors of drug-target interactions reveal kinase inhibitor specificities in living cells

Mikko Taipale, Irina Krykbaeva, Luke Whitesell, Sandro Santagata, Jianming Zhang, Qingsong Liu, Nathanael S Gray & Susan Lindquist

The interaction between the HSP90 chaperone and its client kinases is sensitive to the conformational status of the kinase, and stabilization of the kinase fold by small molecules strongly decreases chaperone interaction. Here we exploit this observation and assay small-molecule binding to kinases in living cells, using chaperones as 'thermodynamic sensors'. The method allows determination of target specificities of both ATP-competitive and allosteric inhibitors in the kinases' native cellular context in high throughput. We profile target specificities of 30 diverse kinase inhibitors against >300 kinases. Demonstrating the value of the assay, we identify ETV6-NTRK3 as a target of the FDA-approved drug crizotinib (Xalkori). Crizotinib inhibits proliferation of ETV6-NTRK3-dependent tumor cells with nanomolar potency and induces the regression of established tumor xenografts in mice. Finally, we show that our approach is applicable to other chaperone and target classes by assaying HSP70/steroid hormone receptor and CDC37/kinase interactions, suggesting that chaperone interactions will have broad application in detecting drug-target interactions *in vivo*.

Nathen:

Reinitiation and Other Unconventional Posttermination Events during Eukaryotic Translation

Molecular Cell, [Volume 51, Issue 2](#), 249-264, 27 June 2013

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10.1016/j.molcel.2013.05.026

Authors

Maxim A. Skabkin, Olga V. Skabkina, Christopher U.T. Hellen, Tatyana V. Pestova

- Highlights
- eIF2, eIF3, eIF1, and eIF1A promote bidirectional reinitiation by recycled 40S subunits
- Imposition of 3' directionality on reinitiation additionally requires eIF4F
- Posttermination 80S ribosomes are mobile and can migrate to cognate codons
- eEF2 induces dissociation of eRF1 and promotes 80S ribosomal migration

Summary

During ribosome recycling, posttermination complexes are dissociated by ABCE1 and eRF1 into 60S and tRNA/mRNA-associated 40S subunits, after which tRNA and mRNA are released by eIF1/eIF1A, Ligatin, or MCT-1/DENR. Occasionally, 40S subunits remain associated with mRNA and reinitiate at nearby AUGs. We recapitulated reinitiation using a reconstituted mammalian translation system. The presence of eIF2, eIF3, eIF1, eIF1A, and Met-tRNA_i^{Met} was sufficient for recycled 40S subunits to remain on mRNA, scan bidirectionally, and reinitiate at upstream and downstream AUGs if mRNA regions flanking the stop codon were unstructured. Imposition of 3' directionality additionally required eIF4F. Strikingly, posttermination ribosomes were not stably anchored on mRNA and migrated bidirectionally to codons cognate to the P site tRNA. Migration depended on the mode of peptide release (puromycin > eRF1-eRF3) and nature of tRNA and was enhanced by eEF2. The mobility of posttermination ribosomes suggests that some reinitiation events could involve 80S ribosomes rather than 40S subunits.

Liyuan:

Diurnal Changes of Polysome Loading Track Sucrose Content in the Rosette of Wild-Type Arabidopsis and the StarchlesspgmMutant

Sunil Kumar Pal, Magdalena Liput, Maria Piques, Hirofumi Ishihara, Toshihiro Obata, Marina C.M. Martins, Ronan Sulpice, Joost T. van Dongen, Alisdair R. Fernie, Umesh Prasad Yadav, John E. Lunn, Björn Usadel, and Mark Stitt*

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Growth is driven by newly fixed carbon in the light, but at night it depends on reserves, like starch, that are laid down in the light. Unless plants coordinate their growth with diurnal changes in the carbon supply, they will experience acute carbon starvation during the night. Protein synthesis represents a major component of cellular growth. Polysome loading was investigated during the diurnal cycle, an extended night, and low CO₂ in Arabidopsis (*Arabidopsis thaliana*) Columbia (Col-0) and in the starchlessphosphoglucosyltransferase (pgm) mutant. In Col-0, polysome loading was 60% to 70% in the light, 40% to 45% for much of the night, and less than 20% in an extended night, while inpgm, it fell to less than 25% early in the night. Quantification of ribosomal RNA species using quantitative reverse transcription-polymerase chain reaction revealed that polysome loading remained high for much of the night in the cytosol, was strongly light dependent in the plastid, and was always high in mitochondria. The rosette sucrose content correlated with overall and with cytosolic polysome loading. Ribosome abundance did not show significant diurnal changes. However, compared with Col-0,pgmhad decreased and increased abundance of plastidic and

mitochondrial ribosomes, respectively. Incorporation of label from CO₂ into protein confirmed that protein synthesis continues at a diminished rate in the dark. Modeling revealed that a decrease in polysome loading at night is required to balance protein synthesis with the availability of carbon from starch breakdown. Costs are also reduced by using amino acids that accumulated in the previous light period. These results uncover a tight coordination of protein synthesis with the momentary supply of carbon.

PROTEOMIC ANALYSIS OF SUMOYLATION IN ARABIDOPSIS THALIANA.

Therese Rytz, Richard Vierstra, Mark Scalf, and Lloyd Smith

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The post-translational modification of proteins by Small Ubiquitin-like Modifier (SUMO) is an essential cellular process in eukaryotes, with genetic studies indicating that it plays a critical role in protection against numerous environmental challenges. Using proteomic methods, we recently identified hundreds of SUMO targets in Arabidopsis that are involved in a wide array of nuclear events, including transcription, chromatin remodelling, and RNA biology, suggesting that SUMOylation provides a rapid and robust mechanism for regulating nuclear activities during stress. Upon exposure to heat shock and other abiotic stresses, the SUMOylation level of some of these proteins increases dramatically and reversibly, especially for those involved in RNA-dependent processes. In addition, modification of SUMO by itself, as well as by ubiquitin, was also detected. To identify the sites of SUMO addition and connect components of the SUMOylation machinery to individual targets, we report here two different mass spectrometric (MS) approaches using Arabidopsis. One is to use a novel technique to detect SUMOylation sites by MS that employs a 6His-tagged lysine-null (K0) SUMO1 construct combined with an alternative peptidase cleavage. This method allows for the exclusive purification of peptides containing a SUMOylation footprint, which enhances MS mapping of conjugation sites by reducing sample complexity. Importantly, we found that the lethal SUMO1/2 double mutant can be rescued with K0 SUMO1, indicating that this lysine-less variant is functionally normal. The wild-type activity of K0 SUMO1, which presumably cannot be modified with either SUMO or ubiquitin, also implies that polySUMO chain formation and SUMO ubiquitylation are not essential. Second, we are combining null mutants of the SUMO E3 ligases SIZ1 and MMS21 with MS analysis of the SUMOylome to link these E3s to specific targets. Ultimately, mapping of SUMOylation sites and identification of corresponding ligases will help in-depth studies of individual SUMO targets and their roles during stress.

The inter-regulation of the unfolded protein response and physiological regulation.

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Endoplasmic reticulum (ER) plays fundamental roles in cellular processes by serving as an entry point for protein trafficking and the frontline of protein quality control system. The protein folding in the ER is tightly monitored by a signaling network termed unfolded protein response (UPR). The UPR is provoked by the overload of unfolded ER proteins, a condition known as ER stress. To compensate the protein folding ability of the ER, the UPR augments transcription of genes encoding ER-resident protein chaperones. In yeast, IRE1 is the only known UPR sensor and conserved in multicellular organisms.

The Arabidopsis genome encodes two IRE1 sequence homologs, AtIRE1A and AtIRE1B. We prove that AtIRE1A and AtIRE1B have overlapping functions that are essential for the plant UPR. *atire1a atire1b* double mutant displays reduced ER stress tolerance and a compromised UPR activation phenotype. We have also established that Arabidopsis AGB1, a subunit of the ubiquitous heterotrimeric GTP-binding protein family, and AtIRE1A/AtIRE1B independently control two essential plant UPR pathways.

The double mutant exhibits a short root phenotype that is enhanced by an *agb1* loss-of-function mutation, underscoring a role for the UPR transducer in organ growth regulation. Although the UPR is essential for multiple developmental processes, the molecular mechanisms that integrate the UPR with physiological processes remain elusive. Recently, we uncover an unexpected genetic interaction between AtIRE1s and key molecular players in both UPR and physiological responses.

We show that the ER stress modulates the developmental signaling at multiple levels and AtIRE1s are required for the specific cellular response. Together we demonstrate that plants have evolved a novel strategy for coordinating the UPR with physiological processes. In contrast to animals, plants, as sessile organisms, have an extraordinary flexibility in post-embryonic development, responding to both internal and external cues. Nonetheless, our understanding of how plants integrate developmental and environmental signals to balance growth and adaptive regulation is limited. The interregulation between the UPR and physiological response demonstrated in this study highlights a plant-specific strategy that evolved to maintain the crucial balance between stress adaptation and growth regulation for ultimate fitness.

Keith:

Turning catalytically inactive human Argonaute proteins into active slicer enzymes

Nature Structural & Molecular Biology 20, 814–817 (2013)

Judith Hauptmann, Anne Dueck, Simone Harlander, Janina Pfaff, Rainer Merkl & Gunter Meister

Biochemistry Center Regensburg, Laboratory for RNA Biology, University of Regensburg, Regensburg, Germany. Institute of Biophysics and Physical Biochemistry, University of Regensburg, Regensburg, Germany.

Argonaute proteins interact with small RNAs that guide them to complementary target RNAs, thus leading to inhibition of gene expression. Some but not all Argonaute proteins are endonucleases and can cleave the complementary target RNA. Here, we have mutated inactive human Ago1 and Ago3 and generated catalytic Argonaute proteins. We find that two short sequence elements at the N terminus are important for activity. In addition, PIWI-domain mutations in Ago1 may misarrange the catalytic center. Our work helps in understanding of the structural requirements that make an Argonaute protein an active endonucleolytic enzyme.

Cigarette Smoke Component Acrolein Modulates Chromatin Assembly by Inhibiting Histone Acetylation

July 26, 2013 *The Journal of Biological Chemistry*, 288, 21678-21687.

Danqi Chen, Lei Fang, Hongjie Li, Moon-shong Tang and Chunyuan Jin

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Chromatin structure and gene expression are both regulated by nucleosome assembly. How environmental factors influence histone nuclear import and the nucleosome assembly pathway, leading to changes in chromatin organization and transcription, remains unknown. Acrolein (Acr) is an α,β -unsaturated aldehyde, which is abundant in the environment, especially in cigarette smoke. It has recently been implicated as a potential major carcinogen of smoking-related lung cancer. Here we show that Acr forms adducts with histone proteins in vitro and in vivo and preferentially reacts with free histones rather than with nucleosomal histones. Cellular fractionation analyses reveal that Acr exposure specifically inhibits acetylations of N-terminal tails of cytosolic histones H3 and H4, modifications that are important for nuclear import and chromatin assembly. Notably, Acr exposure compromises the delivery of histone H3 into chromatin and increases chromatin accessibility. Moreover, changes in nucleosome occupancy at several genomic loci are correlated with transcriptional responses to Acr exposure. Our data provide new insights into mechanisms whereby environmental factors interact with the genome and influence genome function.

Elizabeth:

Cell: Alert 16 July-22 July

[Sulfur Amino Acids Regulate Translational Capacity and Metabolic Homeostasis through Modulation of tRNA Thiolation](#) Original Research Article

Pages 416-429

Sunil Laxman, Benjamin M. Sutter, Xi Wu, Sujai Kumar, Xiaofeng Guo, David C. Trudgian, Hamid Mirzaei, Benjamin P. Tu Protein translation is an energetically demanding process that must be regulated in response to changes in nutrient availability. Herein, we report that intracellular methionine and cysteine availability directly controls the thiolation status of wobble-uridine (U₃₄) nucleotides present on lysine, glutamine, or glutamate tRNAs to regulate cellular translational capacity and metabolic homeostasis. tRNA thiolation is important for growth under nutritionally challenging environments and required for efficient translation of genes enriched in lysine, glutamine, and glutamate codons, which are enriched in proteins important for translation and growth-specific processes. tRNA thiolation is downregulated during sulfur starvation in order to decrease sulfur consumption and growth, and its absence leads to a compensatory increase in enzymes involved in methionine, cysteine, and lysine biosynthesis. Thus, tRNA thiolation enables cells to modulate translational capacity according to the availability of sulfur amino acids, establishing a functional significance for this conserved tRNA nucleotide modification in cell growth control.

[SnapShot: Pathobiology of Alzheimer's Disease](#)

Pages 468-468.e1

Dennis J. Selkoe

Molecular Cell: Alert 16 July-22 July

[Reinitiation and Other Unconventional Posttermination Events during Eukaryotic Translation](#) Original Research Article

Pages 249-264

Maxim A. Skabkin, Olga V. Skabkina, Christopher U.T. Hellen, Tatyana V. Pestova

BÄ¶ttinger L, Guiard B, Oeljeklaus S, Kulawiak B, Zufall N, Wiedemann N, Warscheid B, van der Laan M, Becker T.

A complex of Cox4 and mitochondrial Hsp70 plays an important role in the assembly of the cytochrome c oxidase.

Mol Biol Cell. 2013 Jul 17;. [Epub ahead of print]

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Plant calcium-permeable channels.

Plant Physiol. 2013 Jul 16;. [Epub ahead of print]

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PLoS One. 2013;8(7):e66446.
PMID: 23861744 [PubMed - in process]

Cell: Alert 22 July-28 July

[Deubiquitinases Sharpen Substrate Discrimination during Membrane Protein Degradation from the ER](#) Original Research Article

Zai-Rong Zhang, Juan S. Bonifacino, Ramanujan S. Hegde

Current Biology: Alert 20 July-26 July

[Auxin Controls Gravitropic Setpoint Angle in Higher Plant Lateral Branches](#)

Suruchi Roychoudhry, Marta Del Bianco, Martin Kieffer, Stefan Kepinski

[Artificial microRNAs reveal cell-specific differences in small RNA activity in pollen](#)

Pages R599-R601

Robert Grant-Downton, Sofia Kourmpetli, Said Hafidh, Hoda Khatab, Gael Le Trionnaire, Hugh Dickinson, David Twell

Science Table of Contents for 26 July 2013; Vol. 341, No. 6144

[FtsZ Protofilaments Use a Hinge-Opening Mechanism for Constrictive Force Generation](#)

Ying Li *et al.*

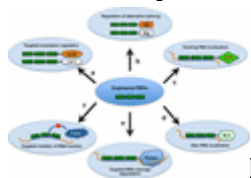
The curved structure of a protein involved in cell division reveals the mechanism for Z-ring constriction during cytokinesis.

FEBS Journal Content Alert: 280, 16 (August 2013)

[Engineering RNA-binding proteins for biology \(pages 3734–3754\)](#)

Yu Chen and Gabriele Varani

Article first published online: 5 JUL 2013 | DOI: 10.1111/febs.12375

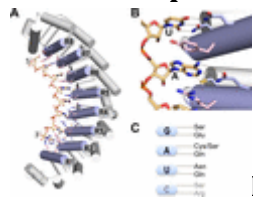


RNA-binding proteins play essential roles in the regulation of gene expression. Many have modular structures and combine relatively few common domains to recognize RNA sequences and/or structures. Based on their structures, the suitability of different RNA-binding domains for engineering RNA-binding specificity is discussed here. Designer RNA-binding proteins will provide valuable tools for biochemical research as well as potential therapeutic applications.

[Engineered proteins with Pumilio/fem-3 mRNA binding factor scaffold to manipulate RNA metabolism \(pages 3755–3767\)](#)

Yang Wang, Zefeng Wang and Traci M. Tanaka Hall

Article first published online: 24 JUN 2013 | DOI: 10.1111/febs.12367



Pumilio/*fem-3* mRNA binding factor (FBF) proteins are characterized by a sequence-specific RNA-binding domain. This unique single-stranded RNA recognition module, whose sequence specificity can be reprogrammed, has been fused with functional modules to engineer protein factors with various functions. Here we summarize the advancement in developing RNA regulatory tools and opportunities for the future.

Nature 499, 379 (25 July 2013) doi:10.1038/499379b

Researchers must continue to lobby politicians, funding agencies and the pharmaceutical industry over the need to implement effective means to curtail the rampant spread of resistance, and to address the glaring dearth of new antibiotics in the drug-development pipeline.

Nature contents: 25 July 2013

The initiation of mammalian protein synthesis and mRNA scanning mechanism

[Ivan B. Lomakin](#) & [Thomas A. Steitz](#)

Nature (2013) doi:10.1038/nature12355

Published online 21 July 2013

During translation initiation in eukaryotes, the small ribosomal subunit binds messenger RNA at the 5' end and scans in the 5' to 3' direction to locate the initiation codon, form the 80S initiation complex and start protein synthesis. This simple, yet intricate, process is guided by multiple initiation factors. Here we determine the structures of three complexes of the small ribosomal subunit that represent distinct steps in mammalian translation initiation. These structures reveal the locations of eIF1, eIF1A, mRNA and initiator transfer RNA bound to the small ribosomal subunit and provide insights into the details of translation initiation specific to eukaryotes. Conformational changes associated with the captured functional states reveal the dynamics of the interactions in the P site of the ribosome. These results have functional implications for the mechanism of mRNA scanning.

The oil palm *SHELL* gene controls oil yield and encodes a homologue of *SEEDSTICK* ▶

Rajinder Singh, Eng-Ti Leslie Low, Leslie Cheng-Li Ooi *et al.*

Genetic mapping and whole-genome sequencing studies identify the *SHELL* gene (a homologue of *Arabidopsis SEEDSTICK*) as responsible for the three different fruit forms in oil palm (*Elaeis guineensis*); this has important economic implications for modulating *SHELL* activity to breed desired fruit forms and enhance oil yields.

Structure of class B GPCR corticotropin-releasing factor receptor 1

Kaspar Hollenstein, James Kean, Andrea Bortolato, Robert K. Y. Cheng, Andrew S. Doré [+ et al.](#)

Approximately 30% of known drugs target G protein-coupled receptors (GPCRs), but all the published structures of GPCRs to date are from the class A family of GPCRs; here the first X-ray crystal structure of a member of the class B family of GPCRs, the human corticotropin-releasing factor receptor 1, is determined.

Physiologia Plantarum Content Alert (New Articles)

Chloroplast-targeted Hsp90 plays essential roles in plastid development and embryogenesis in Arabidopsis possibly linking with VIPP1

Juanjuan Feng, Pengxiang Fan, Ping Jiang, Sulian Lv, Xianyang Chen and Yinxin Li

Accepted manuscript online: 22 JUL 2013 12:49PM EST | DOI: 10.1111/ppl.12083

Journal of Agronomy and Crop Sci... Content Alert (New Articles)

Heat Stress

Genetic Variation for Heat Tolerance During the Reproductive Phase in *Brassica rapa*

Annisa, S. Chen, N. C. Turner and W. A. Cowling

Article first published online: 19 JUL 2013 | DOI: 10.1111/jac.12034

Spatial and Temporal Analysis of NADPH Oxidase-Generated Hydrogen

Peroxide Signals by Novel Fluorescent Reporter Proteins

Balázs Enyedi, Melinda Zana, Ágnes Donkó, and Miklós Geiszt

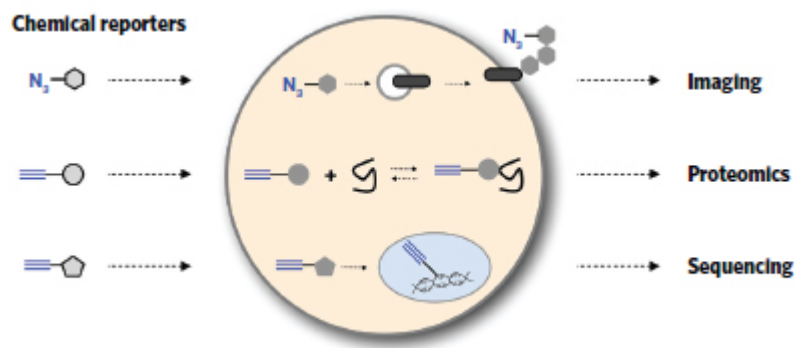
Antioxidants & Redox Signaling,
Vol. 19, No. 6, August 2013: 523-534.

Nature Chemical Biology Contents: August 2013 Volume 9 Number 8 pp 468 - 526

Chemical reporters for biological discovery pp475 - 484

Markus Grammel and Howard C Hang

doi:10.1038/nchembio.1296



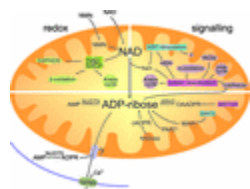
Bioorthogonal chemistry, facilitated by enzymatic incorporation of chemical reporters *in vitro* or in cells, permits selective labeling and visualization of proteins, nucleic acids and other biomolecules such as glycans and lipids and facilitates the interrogation of their cellular functions.

FEBS Journal Content Alert: 280, 15 (August 2013)

NAD and ADP-ribose metabolism in mitochondria (pages 3530–3541)

Christian Dölle, Johannes G.M. Rack and Mathias Ziegler

Article first published online: 3 JUN 2013 | DOI: 10.1111/febs.12304

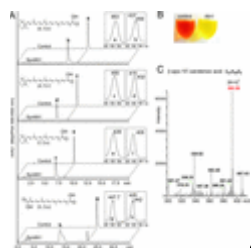


NAD plays an essential role in mitochondria as redox cofactor and substrate for signalling reactions. NAD dependent signalling involves degradation of the nucleotide and conversion to ADP-ribose derivatives including second messenger generation and posttranslational protein modifications. The major NAD dependent reactions within mitochondria, their metabolic and regulatory function, and fate of NAD degradation products are highlighted.

The ORF *slr0091* of *Synechocystis* sp. PCC6803 encodes a high-light induced aldehyde dehydrogenase converting apocarotenals and alkanals (pages 3685–3696)

Danika Trautmann, Peter Beyer and Salim Al-Babili

Article first published online: 5 JUL 2013 | DOI: 10.1111/febs.12361



Aldehyde dehydrogenases play an important role in detoxification of reactive aldehydes. Here, we report on a cyanobacterial enzyme capable in converting two classes of lipid-derived aldehydes, apocarotenals and alkanals. The corresponding gene is a constituent of a stress-related operon, and homology to eukaryotic enzymes points to a yet not considered possibility of their being involved in scavenging of apocarotenals.

King AM, Toxopeus J, Macrae TH.

Functional Differentiation of Small Heat Shock Proteins in Diapause-Destined *Artemia* Embryos.

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PMID: 23879561 [PubMed - as supplied by publisher]

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ATP-driven molecular chaperone machines.

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Curr Opin Plant Biol. 2013 Jul 20;. [Epub ahead of print]

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A novel *Arabidopsis* MYB-like transcription factor, MYBH, regulates hypocotyl elongation by enhancing auxin accumulation.

J Exp Bot. 2013 Jul 25;. [Epub ahead of print]

PMID: 23888064 [PubMed - as supplied by publisher]

Nature Chemical Biology

Metabolomics: Playing piñata with single cells - pp471 - 473

Oscar Yanes

doi:10.1038/nchembio.1297

Mass spectrometry advances in single-cell metabolomics enable the discovery of a new biological insight that is not accessible from population-level studies. A new study reveals that single baker's yeast cells provide sufficient material to study chemical and genetic inhibition of glycolysis and identifies metabolic subpopulations that would be invisible in bulk.

Nature Genetics Contents: August 2013 pp 843 - 962

Massive genomic variation and strong selection in Arabidopsis thaliana lines from Sweden pp884 - 890

Quan Long, Fernando A Rabanal, Dazhe Meng, Christian D Huber, Ashley Farlow, Alexander Platzer, Qingrun Zhang, Bjarni J Vilhjálmsson, Arthur Korte, Viktoria Nizhynska, Viktor Voronin, Pamela

Korte, Laura Sedman, Terezie Mandáková, Martin A Lysak, Ümit Seren, Ines Hellmann & Magnus Nordborg

doi:10.1038/ng.2678

Magnus Nordborg and colleagues report sequencing of 180 *Arabidopsis thaliana* lines from Sweden. They characterize patterns of genetic variation and selection and provide a population resource that will be useful for association studies.

An atlas of over 90,000 conserved noncoding sequences provides insight into crucifer regulatory regions **OPEN** pp891 - 898

Annabelle Haudry, Adrian E Platts, Emilio Vello, Douglas R Hoen, Mickael Leclercq, Robert J Williamson, Ewa Forczek, Zoé Joly-Lopez, Joshua G Steffen, Khaled M Hazzouri, Ken Dewar, John R Stinchcombe, Daniel J Schoen, Xiaowu Wang, Jeremy Schmutz, Christopher D Town, Patrick P Edger, J Chris Pires, Karen S Schumaker, David E Jarvis, Terezie Mandáková, Martin A Lysak, Erik van den Bergh, M Eric Schranz, Paul M Harrison, Alan M Moses, Thomas E Bureau, Stephen I Wright & Mathieu Blanchette

doi:10.1038/ng.2684

Mathieu Blanchette and colleagues report whole-genome sequencing of three Brassicaceae species, *Leavenworthia alabamica*, *Sisymbrium irio* and *Aethionema arabicum*. They include comparative genomic analysis with 6 additional crucifer genomes, identify and characterize over 90,000 conserved noncoding sequences and provide a map of functional noncoding regions in plant genomes.