

**Damian:**

1) Interaction of Circadian Clock Proteins CRY1 and PER2 Is Modulated by Zinc Binding and Disulfide Bond Formation

Ira Schmalen, Silke Reischl, Thomas Wallach, Roman Klemz, Astrid Grudziecki, J. Rajan Prabu, Christian Benda, Achim Kramer, and Eva Wolf  
*Cell* 157, 1203–1215, May 22, 2014

2) Dissecting common  $\gamma$  chain cytokine family signaling in T cells using cell-to-cell variability analysis

Jesse W. Cotari, Guillaume Voisinne, Orly Even Dar, Volkan Karabacak, and Grégoire Altan-Bonnet  
*Sci Signal.* ; 6(266): ra17. doi:10.1126/scisignal.2003240.

3) Evolution at protein ends: major contribution of alternative transcription initiation and termination to the transcriptome and proteome diversity in mammals

Svetlana A. Shabalina, Aleksey Y. Ogurtsov, Nikolay A. Spiridonov, and Eugene V. Koonin  
*Nucleic Acids Research*, 2014 1 doi: 10.1093/nar/gku342

**Indu:**

1. Science. 2014 May 9;344(6184):1250494. doi: 10.1126/science.1250494.

Structural basis for protein antiaggregation activity of the trigger factor chaperone.

Saio T(1), Guan X, Rossi P, Economou A, Kalodimos CG.

Author information:

(1)Center for Integrative Proteomics Research and Department of Chemistry and Chemical Biology, Rutgers University, Piscataway, NJ 08854, USA.

Comment in

Science. 2014 May 9;344(6184):590-1.

Molecular chaperones prevent aggregation and misfolding of proteins, but scarcity of structural data has impeded an understanding of the recognition and antiaggregation mechanisms. We report the solution structure, dynamics, and energetics of three trigger factor (TF) chaperone molecules in complex with alkaline phosphatase (PhoA) captured in the unfolded state. Our data show that TF uses multiple sites to bind to several regions of the PhoA substrate protein primarily through hydrophobic contacts. Nuclear magnetic resonance (NMR) relaxation experiments show that TF interacts with PhoA in a highly dynamic fashion, but as the number and length of the PhoA regions engaged by TF increase, a more stable complex gradually emerges. Multivalent binding keeps the substrate protein in an extended, unfolded conformation. The results show how molecular

chaperones recognize unfolded polypeptides and, by acting as unfoldases and holdases, prevent the aggregation and premature (mis) folding of unfolded proteins.

PMID: 24812405 [PubMed - indexed for MEDLINE]

2. Science. 2014 May 9;344(6184):638-41. doi: 10.1126/science.1250498.

Gibberellin acts positively then negatively to control onset of flower formation in Arabidopsis.

Yamaguchi N(1), Winter CM, Wu MF, Kanno Y, Yamaguchi A, Seo M, Wagner D.

Author information:

(1)Department of Biology, University of Pennsylvania, 415 South University Avenue, Philadelphia, PA 19104-6018, USA.

The switch to reproductive development is biphasic in many plants, a feature important for optimal pollination and yield. We show that dual opposite roles of the phytohormone gibberellin underpin this phenomenon in Arabidopsis. Although gibberellin promotes termination of vegetative development, it inhibits flower formation. To overcome this effect, the transcription factor LEAFY induces expression of a gibberellin catabolism gene; consequently, increased LEAFY activity causes reduced gibberellin levels. This allows accumulation of gibberellin-sensitive DELLA proteins. The DELLA proteins are recruited by SQUAMOSA PROMOTER BINDING PROTEIN-LIKE transcription factors to regulatory regions of the floral commitment gene APETALA1 and promote APETALA1 up-regulation and floral fate synergistically with LEAFY. The two opposing functions of gibberellin may facilitate evolutionary and environmental modulation of plant inflorescence architecture.

PMID: 24812402 [PubMed - indexed for MEDLINE]

3. Science. 2014 May 16;344(6185):711-6. doi: 10.1126/science.1251358.

Border control--a membrane-linked interactome of Arabidopsis.

Jones AM(1), Xuan Y(1), Xu M(1), Wang RS(2), Ho CH(1), Lalonde S(1), You CH(1), Sardi MI(1), Parsa SA(1), Smith-Valle E(1), Su T(1), Frazer KA(1), Pilot G(3), Pratelli R(3), Grossmann G(1), Acharya BR(4), Hu HC(5), Engineer C(6), Villiers F(5), Ju C(5), Takeda K(5), Su Z(4), Dong Q(7), Assmann SM(4), Chen J(8), Kwak JM(9), Schroeder JI(6), Albert R(2), Rhee SY(10), Frommer WB(10).

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Cellular membranes act as signaling platforms and control solute transport. Membrane receptors, transporters, and enzymes communicate with intracellular processes through protein-protein interactions. Using a split-ubiquitin yeast two-hybrid screen that covers a test-space of  $6.4 \times 10^6$  pairs, we identified 12,102 membrane/signaling protein interactions from Arabidopsis. Besides confirmation of expected interactions such as heterotrimeric G protein subunit interactions and aquaporin oligomerization, >99% of the interactions were previously unknown. Interactions were confirmed at a rate of 32% in orthogonal in planta split-green fluorescent protein interaction assays, which was statistically indistinguishable from the confirmation rate for known interactions collected from literature (38%). Regulatory associations in membrane protein trafficking, turnover, and phosphorylation include regulation of potassium channel activity through abscisic acid signaling, transporter activity by a WNK kinase, and a brassinolide receptor kinase by trafficking-related proteins. These examples underscore the utility of the membrane/signaling protein interaction network for gene discovery and hypothesis generation in plants and other organisms.

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PMID: 24833385 [PubMed - in process]

### **Elizabeth:**

LIX+New Journal to be launched in 2015: ***NATURE PLANTS***

*Nature Plants* is concerned with all aspects of plants be it their evolution, development or metabolism, their interactions with the environment, or their societal significance.

Publishing monthly it will have a particular interest in studies that advance knowledge and inform development across a diversity of areas

*Nature Plants* is committed to publishing primary research into the molecular biology, physiology and ecology of plants—in both the basic and applied research spheres—as well as investigations into the relationship between humanity and the plant

kingdom. In so doing, *Nature Plants* will provide a fully rounded picture of the most accomplished and significant advances in the plant sciences.

Excellent source of info on status of CRISPR technology – though not much from plants.

<http://www.addgene.org/CRISPR/guide/>

The Plant Journal Content Alert: 78, 5 (June 2014)

**Precise plant breeding using new genome editing techniques: opportunities, safety and regulation in the EU (pages 742–752)**

Frank Hartung and Joachim Schiemann

Article first published online: 3 FEB 2014 | DOI: 10.1111/tpj.12413

**Nature contents: 29 May 2014**

**Accurate design of co-assembling multi-component protein nanomaterials**

[Neil P. King](#), [Jacob B. Bale](#), [William Sheffler](#), [Dan E. McNamara](#), [Shane Gonen](#), [Tamir Gonen](#), [Todd O. Yeates](#) & [David Baker](#)

The self-assembly of proteins into highly ordered nanoscale architectures is a hallmark of biological systems. The sophisticated functions of these molecular machines have inspired the development of methods to engineer self-assembling protein nanostructures; however, the design of multi-component protein nanomaterials with high accuracy remains an outstanding challenge. Here we report a computational method for designing protein nanomaterials in which multiple copies of two distinct subunits co-assemble into a specific architecture. We use the method to design five 24-subunit cage-like protein nanomaterials in two distinct symmetric architectures and experimentally demonstrate that their structures are in close agreement with the computational design models. The accuracy of the method and the number and variety of two-component materials that it makes accessible suggest a route to the construction of functional protein nanomaterials tailored to specific applications.

Nature 509, 582–587 (29 May 2014) doi:10.1038/nature13319

**Mass-spectrometry-based draft of the human proteome**

[Mathias Wilhelm](#), [Judith Schlegl](#), [Hannes Hahne](#), [Amin Moghaddas Gholami](#), [Marcus Lieberenz](#), [Mikhail M. Savitski](#), et al

Proteomes are characterized by large protein-abundance differences, cell-type- and time-dependent expression patterns and post-translational modifications, all of which carry biological information that is not accessible by genomics or transcriptomics. Here we present a mass-spectrometry-based draft of the human proteome and a public, high-performance, in-memory database for real-time analysis of terabytes of big data, called ProteomicsDB. The information assembled from human tissues, cell lines and body fluids enabled estimation of the size of the protein-coding genome, and identified organ-specific proteins and a large number of translated lincRNAs (long intergenic non-coding RNAs). Analysis of messenger RNA and protein-expression profiles of human tissues revealed conserved control of protein abundance, and integration of drug-sensitivity data enabled the identification of proteins predicting resistance or sensitivity. The proteome profiles also hold considerable promise for analysing the composition and stoichiometry of protein complexes. ProteomicsDB thus enables navigation of proteomes, provides biological insight and fosters the development of proteomic technology.

Antioxidants & Redox Signaling. June 20, 2014, 20(18): 2891-2906.

## Aggregate-Prone R120GCRYAB Triggers Multifaceted Modifications of the Thioredoxin System

Banerjee MustafiSoumyajit, GroseJulianne H., ZhangHuali, PrattGregory W., SadoshimaJunichi, ChristiansElisabeth S., and BenjaminIvor J..

**Aims:** The human mutation R120G in the  $\alpha$ B-crystallin (CRYAB) causes a multisystemic disease that is characterized by hypertrophic cardiomyopathy and cytoplasmic protein aggregates. In transgenic mice, human R120GCRYAB (hR120GTg) expression in heart sequentially modifies the REDOX status, in part by the activation of the nuclear factor, erythroid derived 2, like 2 (*Nrf2*). Thioredoxin system (TS) components are NRF2 target genes, so it could be hypothesized that TS was affected in hR120GTg mice. **Results:** Transgenic hearts overexpressed thioredoxin 1 (Trx1), which was identified by isotope coded affinity tag-mass spectrometry, among hundreds of peptides displaying an increased reduced/oxidized ratio. Coupled to this higher level of reduced cysteines, the activity of thioredoxin reductase 1 (TrxR1) was augmented by 2.5-fold. Combining multiple experimental approaches, the enzymatic regulation of TrxR1 by a histone deacetylase 3 (HDAC3)-dependent level of acetylation was confirmed. *In vitro* and *in vivo* functional tests established that TrxR1 activity is required to mitigate aggregate development, and this could be mediated by Bcl-2-associated athanogene 3 (BAG3) as a potential TS substrate. **Innovation and Conclusions:** This study uncovers the compartmentalized changes and the involvement of TS in the cardiac stress response elicited by misfolded proteins such as R120GCRYAB. Our work suggests that R120GCRYAB triggers a defensive pathway acting through the newly identified interacting partners HDAC3, TrxR1, and BAG3 to counter aggregate growth. Therefore, those interactors may function as modifier genes contributing to the variable onset and expressivity of such human diseases. Furthermore, our work underscores the potential organismal effects of pharmacological interventions targeting TS and HDAC. *Antioxid. Redox Signal.* 20, 2891–2906.

*Antioxidants & Redox Signaling.* June 20, 2014, 20(18): 2923-2935.  
doi:10.1089/ars.2013.5553.

## Protein S-nitrosylation in *Plasmodium falciparum*

WangLihui, DelahuntyClaire, PrietoJudith Helena, RahlfsStefan, JortzikEsther, YatesJohn R.III, and BeckerKatja.

**Aims:** Due to its life in different hosts and environments, the human malaria parasite *Plasmodium falciparum* is exposed to oxidative and nitrosative challenges. Nitric oxide (NO) and NO-derived reactive nitrogen species can constitute nitrosative stress and play a major role in NO-related signaling. However, the mode of action of NO and its targets in *P. falciparum* have hardly been characterized. Protein S-nitrosylation (SNO), a posttranslational modification of protein cysteine thiols, has emerged as a principal mechanism by which NO exerts diverse biological effects. Despite its potential importance, SNO has hardly been studied in human malaria parasites. Using a biotin-switch approach coupled to mass spectrometry, we systemically studied SNO in *P. falciparum* cell extracts. **Results:** We identified 319 potential targets of SNO that are widely distributed throughout various cellular pathways. Glycolysis in the parasite was found to be a major target, with glyceraldehyde-3-phosphate dehydrogenase being strongly inhibited by S-nitrosylation of its active site cysteine. Furthermore, we show that *P. falciparum* thioredoxin 1 (PfTrx1) can be S-nitrosylated at its nonactive site cysteine

(Cys43). Mechanistic studies indicate that PfTrx1 possesses both denitrosylating and transnitrosylating activities mediated by its active site cysteines and Cys43, respectively. **Innovation:** This work provides first insights into the S-nitrosoproteome of *P. falciparum* and suggests that the malaria parasite employs the thioredoxin system to deal with nitrosative challenges. **Conclusion:** Our results indicate that SNO may influence a variety of metabolic processes in *P. falciparum* and contribute to our understanding of NO-related signaling processes and cytotoxicity in the parasites. *Antioxid. Redox Signal.* 20, 2923–2935.

Antioxidants & Redox Signaling. June 20, 2014, 20(18): 3024-3039.  
doi:10.1089/ars.2013.5530.

### Circadian Redox Signaling in Plant Immunity and Abiotic Stress

Spoel Steven H. and van Ooijen Gerben.

**Significance:** Plant crops are critically important to provide quality food and bio-energy to sustain a growing human population. Circadian clocks have been shown to deliver an adaptive advantage to plants, vastly increasing biomass production by efficient anticipation to the solar cycle. Plant stress, on the other hand, whether biotic or abiotic, prevents crops from reaching maximum productivity. **Recent Advances:** Stress is associated with fluctuations in cellular redox and increased phytohormone signaling. Recently, direct links between circadian timekeeping, redox fluctuations, and hormone signaling have been identified. A direct implication is that circadian control of cellular redox homeostasis influences how plants negate stress to ensure growth and reproduction. **Critical Issues:** Complex cellular biochemistry leads from perception of stress via hormone signals and formation of reactive oxygen intermediates to a physiological response. Circadian clocks and metabolic pathways intertwine to form a confusing biochemical labyrinth. Here, we aim to find order in this complex matter by reviewing current advances in our understanding of the interface between these networks. **Future Directions:** Although the link is now clearly defined, at present a key question remains as to what extent the circadian clock modulates redox, and vice versa. Furthermore, the mechanistic basis by which the circadian clock gates redox- and hormone-mediated stress responses remains largely elusive. *Antioxid. Redox Signal.* 20, 3024–3039.

Nature Genetics Contents: June 2014 pp 523 - 657

### Heterotrimeric G proteins regulate nitrogen-use efficiency in rice pp652 - 656

Hongying Sun, Qian Qian, Kun Wu, Jijing Luo, Shuansuo Wang, Chengwei Zhang, Yanfei Ma, Qian Liu, Xianzhong Huang, Qingbo Yuan, Ruixi Han, Meng Zhao, Guojun Dong, Longbiao Guo, Xudong Zhu, Zhiheng Gou, Wen Wang, Yuejin Wu, Hongxuan Lin & Xiangdong Fu

doi: 10.1038/ng.2958

Xiangdong Fu and colleagues show that variation in *DEP1*, which encodes a G protein subunit known to influence rice panicle architecture, underlies a major quantitative trait locus for nitrogen-use efficiency. These findings suggest that modulating heterotrimeric G protein activity could contribute to environmentally sustainable increases in rice grain yield.

*Science* 16 May 2014: Vol. 344 no. 6185 pp. 687-689

DOI: 10.1126/science.344.6185.687

### The Hunt for Missing Genes

Daniel MacArthur is intrigued by the prospect that hidden in the human population are people who lack certain genes yet remain healthy. Finding such natural human "knockouts" and looking for differences between their physiology and that of people with the intact gene may be the only way to fully understand the function of many of our

genes, he and others contend. It could also have biomedical payoffs. To get started, MacArthur and others want to comb through many thousands of people's genomes for missing genes to seed what MacArthur calls the Human Knockout Project. But identifying dispensable genes is only the start of the challenge.

**Nature Protocols Contents: Volume 9 Number 6, pp 1213-1531**  
**Monitoring protein conformational changes and dynamics using stable-isotope labeling and mass spectrometry pp1301 - 1319**

CDSiL-MS involves labeling cysteine and lysine side chains in proteins with N-ethylmaleimide and succinic anhydride, respectively. Information about the conformational state of the protein is inferred from the labeling kinetics as determined by mass spectrometry.

Alem W Kahsai, Sudarshan Rajagopal, Jinpeng Sun and Kunhong Xiao

Published online: 08 May 2014 | doi: 10.1038/nprot.2014.075

Journal of Plant Physiology: Alert 20 May-26 May

**[Nitric-oxide inhibits nyctinastic closure through cGMP in Albizia lophantha leaflets.](#)** Original Research Article

Available online 23 May 2014

Carmen Bergareche, Luisa Moysset, Alcira Paola Angelo, Samira Chellik, Esther Simón.

**[Dehydration induces expression of GALACTINOL SYNTHASE and RAFFINOSE SYNTHASE in seedlings of pea \(Pisum sativum L.\)](#)** Original Research Article

Available online 17 May 2014

Lesław B. Lahuta, Wioletta E. Pluskota, Joanna Stelmaszewska, Joanna Szablińska

**[Current Opinion in Plant Biology](#)**

**[The chemical logic of plant natural product biosynthesis](#)**

Review Article *Pages 51-58* Gülbenk Anarat-Cappillino, Elizabeth S Sattely

**[Prospects of genetic engineering for robust insect resistance](#)**

Review Article *Pages 59-67* Michael A Birkett, John A Pickett

Archives of Biochemistry and Biophysics: Alert 19 May-25 May

**[Evolution of protein interactions: From interactomes to interfaces](#)** Review Article

Available online 20 May 2014

Jessica Andreani, Raphael Guerois

Hill SM, Hao X, Liu B, Nyström T.

Life-span extension by a metacaspase in the yeast *Saccharomyces cerevisiae*.

Science. 2014 May 22;. [Epub ahead of print]

PMID: 24855027 [PubMed - as supplied by publisher]

Toxopeus J, Warner AH, MacRae TH.

Group 1 LEA proteins contribute to the desiccation and freeze tolerance of *Artemia franciscana* embryos during diapause.

Cell Stress Chaperones. 2014 May 21;. [Epub ahead of print]

PMID: 24846336 [PubMed - as supplied by publisher]

[Curr Biol](#). 2014 May 19;24(10):R453-R462. doi: 10.1016/j.cub.2014.03.034.

**ROS Function in Redox Signaling and Oxidative Stress.**

[Schieber M](#)<sup>1</sup>, [Chandel NS](#)<sup>2</sup>.

Oxidative stress refers to elevated intracellular levels of reactive oxygen species (ROS) that cause damage to lipids, proteins and DNA. Oxidative stress has been linked to a myriad of pathologies. However, elevated ROS also act as signaling molecules in the maintenance of physiological functions - a process termed redox biology. In this review we discuss the two faces of ROS - redox biology and oxidative stress - and their contribution to both physiological and pathological conditions. Redox biology involves a small increase in ROS levels that activates signaling pathways to initiate biological processes, while oxidative stress denotes high levels of ROS that result in damage to DNA, protein or lipids. Thus, the response to ROS displays hormesis, given that the opposite effect is observed at low levels compared with that seen at high levels. Here, we argue that redox biology, rather than oxidative stress, underlies physiological and pathological conditions.

Carroni M, Kummer E, Oguchi Y, Wendler P, Clare DK, Sinning I, Kopp J, Mogk A, Bukau B, Saibil HR.

Head-to-tail interactions of the coiled-coil domains regulate ClpB activity and cooperation with Hsp70 in protein disaggregation.

*Elife*. 2014 Apr 30;3:e02481.

PMID: 24843029 [PubMed]

Liu Z, Yao P, Guo X, Xu B.

Two small heat shock protein genes in *Apis cerana cerana*: characterization, regulation, and developmental expression.

*Gene*. 2014 May 14;. [Epub ahead of print]

PMID: 24835315 [PubMed - as supplied by publisher]

Gamerding M, Deuerling E.

Biochemistry. Trigger factor flexibility.

*Science*. 2014 May 9;344(6184):590-1.

PMID: 24812390 [PubMed - indexed for MEDLINE]

Kenney JW, Moore CE, Wang X, Proud CG.

Eukaryotic elongation factor 2 kinase, an unusual enzyme with multiple roles.

*Adv Biol Regul*. 2014 Apr 30;. [Epub ahead of print]

PMID: 24853390 [PubMed - as supplied by publisher]

Yang F, Gao Y, Li Z, Chen L, Xia Z, Xu T, Qin Y.

Mitochondrial EF4 links respiratory dysfunction and cytoplasmic translation in *Caenorhabditis elegans*.

*Biochim Biophys Acta*. 2014 May 15;. [Epub ahead of print]

PMID: 24837196 [PubMed - as supplied by publisher]

**Current Opinion in Biotechnology: Alert 17 May-23 May**

[Agricultural soils, pesticides and microbial diversity](#) Review Article

Pages 15-20

Carsten Suhr Jacobsen, Mathis Hjort Hjelmso



Annaluru, N., et al. (2014.) *Science* 344, 55–58.

### **Synthetic Chromosome, the Abridged Story**

The recent design and assembly of the first synthetic eukaryotic chromosome (Annaluru et al., 2014) inspires great confidence in our burgeoning ability to engineer life with desired properties and for new purposes. The creation, called synIII (it was modeled on *Saccharomyces cerevisiae* chromosome III), is matched in scale only by previous efforts in bacteria, and its successful assembly issues a declaration that synthetic biologists need not limit their ambitions to noneukaryotes or even to single-celled organisms. While making synIII, the authors introduce a bit of judicious streamlining, removing introns, transposons, subtelomeric regions, and some transfer RNA genes. The authors additionally introduce 98 loxP sites to flank the genes that are known to be individually nonessential in order to enable future study of inducible evolution and genome reduction. With these changes, synIII has a total size of 272,871 base pairs, substantially shorter (by ~44k bp) than its native counterpart that it replaces. Indeed, more than 50,000 bp were deleted, inserted, or changed during the design process, and these are clustered in more than 600 distinct editing events (see image). And yet, the chromosome is fully functional, has no apparent deleterious effect on cell viability, and is also stable across many generations. Its robust functionality, despite these engineered changes, is perhaps the most remarkable facet of the study. The effort is part of a larger consortium project to create the first wholly designer eukaryotic genome. Although much remains left to be done, these results suggest that a synthetic life based on these engineering principles may be viable and thus amenable to additional modifications and experimental control.

Malyshev, D.A., et al. (2014). *Nature*. Published online May 7, 2014. <http://dx.doi.org/10.1038/nature13314>

### **Adding New Letters to the Genetic Alphabet**

Look at a genome, any genome, and what you will see is a nearly endless string of As, Cs, Ts, and Gs. Malyshev et al. (2014) now break this monotony by engineering the bacterium *E. coli* so that it will propagate a pair of unnatural bases. The synthetic bases, known as d5SICS and dNaM, differ from native bases from a chemical standpoint in that their interaction depends predominantly on hydrophobic bonds and not the hydrogen bonds of classic dA-dT and dG-dC pairs. Previous work has shown in vitro that these bases can be incorporated into DNA, transcribed, and amplified by PCR. However, moving them in vivo presents challenges, not least of which is how to ensure that the synthesized nucleotide triphosphates (NTPs) are available for endogenous polymerases. To overcome this hurdle, the authors exogenously express NTP transporters from algae and show that they can mediate import of the unnatural NTPs supplied in the media (and further establish an alteration to the growth media that promotes NTP stability in the bacterial periplasm). From there, the bacterium takes charge, proving impressively adept at using the unnatural NTPs to replicate a plasmid that includes the nonnative base pair. The bacteria appear to grow normally, and the unnatural base pairs are largely retained as the cultures grow, suggesting that the bases are not efficiently removed by DNA repair pathways. So, what's next for the world's first organism to have six letters in its genetic code? The authors forecast the construction of orthogonal transcription networks in engineered cells and, even further down the road, the ability to encode proteins with

unnatural amino acids. Given the complexity possible with a code based on only two pairs of bases, what now, for three?

Nature Reviews Molecular Cell Biology contents June 2014 Volume 15 Number 6 pp 363-426

**The amyloid state and its association with protein misfolding diseases**

*Tuomas P. J. Knowles, Michele Vendruscolo & Christopher M. Dobson*

p384 | doi:10.1038/nrm3810

Protein aggregation and amyloid deposition are associated with a wide range of medical disorders, including Alzheimer's disease and type II diabetes. Studies into the amyloid state are revealing fundamental principles that underlie the maintenance of protein homeostasis, and the origins of aberrant protein behaviour and disease.

**Cellular mechanisms and physiological consequences of redox-dependent signalling**

*Kira M. Holmström & Toren Finkel*

p411 | doi:10.1038/nrm3801

Although they are damaging when produced in large quantities, low levels of reactive oxygen species (ROS) can function within specific signalling pathways, based on the reversible oxidation of crucial Cys residues in reduction-oxidation (redox)-sensitive target proteins. Understanding these pathways has implications for metabolic regulation, innate immunity, stem cell biology, tumorigenesis and ageing.

**Dan:**

PLANT MOLECULAR BIOLOGY

Title:

CRISPR–Cas system: a powerful tool for genome engineering

Abstract:

Targeted gene regulation on a genome-wide scale is a powerful strategy for interrogating, perturbing, and engineering cellular systems. Recent advances with the RNA-mediated Cas9 endonuclease derived from clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated proteins (Cas) systems have dramatically transformed our ability to specifically modify intact genomes of diverse cells and organisms. The CRISPR-Cas system has been adapted as an efficient, facile, and robust gene-targeting technology with the potential for high-throughput and multiplexed genome engineering. Exciting breakthroughs in understanding the mechanisms of the CRISPR-Cas system and its enormous potential for applications across basic science, agricultural and biotechnology.

**Ariel:**

## 1) Greater sensitivity to drought accompanies maize yield increase in the U.S. Midwest.

[Lobell DB](#)<sup>1</sup>, [Roberts MJ](#), [Schlenker W](#), [Braun N](#), [Little BB](#), [Rejesus RM](#), [Hammer GL](#).

A key question for climate change adaptation is whether existing cropping systems can become less sensitive to climate variations. We use a field-level data set on maize and soybean yields in the central United States for 1995 through 2012 to examine changes in drought sensitivity. Although yields have increased in absolute value under all levels of stress for both crops, the sensitivity of maize yields to drought stress associated with high vapor pressure deficits has increased. The greater sensitivity has occurred despite cultivar improvements and increased carbon dioxide and reflects the agronomic trend toward higher sowing densities. The results suggest that agronomic changes tend to translate improved drought tolerance of plants to higher average yields but not to decreasing drought sensitivity of yields at the field scale.

### **Stephanie:**

[Trends Biochem Sci](#). 2014 Jun;39(6):255-7. doi: 10.1016/j.tibs.2014.04.002. Epub 2014 Apr 18.

## Sizing up the poly(A) tail: insights from deep sequencing.

[Zheng D](#)<sup>1</sup>, [Tian B](#)<sup>2</sup>.

### **Author information**

#### **Abstract**

Global investigation of poly(A) tails has been hindered by technical challenges. In a recent advance, two groups developed deep sequencing methods to globally interrogate poly(A) tail length and sequence with high precision, opening new avenues for investigation of poly(A) tail functions in mRNA metabolism. Initial applications of these methods reveal insights into the relationship between poly(A) tail length and translational efficiency, and identify widespread uridylation and guanylation at the 3' ends of transcripts.

### **Keith:**

#### ***1) Arabidopsis AtPARK13, Which Confers Thermotolerance, Targets Misfolded Proteins\****

May 23, 2014 The Journal of Biological Chemistry, 289, 14458-14469.

Indranil Basak<sup>‡</sup>, Ramavati Pal<sup>‡</sup>, Ketan S. Patil<sup>‡</sup>, Aisling Dunne<sup>‡</sup>, Hsin-Pin Ho<sup>§</sup>, Sungsu Lee<sup>‡</sup>, Diluka Peiris<sup>¶</sup>, Jodi Maple-Grødem<sup>||</sup>, Mark Odell<sup>¶</sup>, Emmanuel J. Chang<sup>§</sup>, Jan Petter Larsen<sup>||</sup> and Simon G. Møller<sup>‡,||<sup>1</sup></sup>

‡Department of Biological Sciences, St. John's University, New York, New York 11439,  
§Department of Chemistry, York College of the City University of New York, New York,  
New York 11451, ¶Department of Molecular and Applied Biosciences, University of  
Westminster, London W1W 6UW, United Kingdom, and  
||Norwegian Center for Movement Disorders, Stavanger University Hospital, 4068  
Stavanger, Norway

Mutations in HTRA2/Omi/PARK13 have been implicated in Parkinson disease (PD). PARK13 is a neuroprotective serine protease; however, little is known about how PARK13 confers stress protection and which protein targets are directly affected by PARK13. We have reported that *Arabidopsis thaliana* represents a complementary PD model, and here we demonstrate that AtPARK13, similar to human PARK13 (hPARK13), is a mitochondrial protease. We show that the expression/accumulation of AtPARK13 transcripts are induced by heat stress but not by other stress conditions, including oxidative stress and metals. Our data show that elevated levels of AtPARK13 confer thermotolerance in *A. thaliana*. Increased temperatures accelerate protein unfolding, and we demonstrate that although AtPARK13 can act on native protein substrates, unfolded proteins represent better AtPARK13 substrates. The results further show that AtPARK13 and hPARK13 can degrade the PD proteins  $\alpha$ -synuclein (SNCA) and DJ-1/PARK7 directly, without autophagy involvement, and that misfolded SNCA and DJ-1 represent better substrates than their native counterparts. Comparative proteomic profiling revealed AtPARK13-mediated proteome changes, and we identified four proteins that show altered abundance in response to AtPARK13 overexpression and elevated temperatures. Our study not only suggests that AtPARK13 confers thermotolerance by degrading misfolded protein targets, but it also provides new insight into possible roles of this protease in neurodegeneration.

## **2) Eukaryotic Translation Initiation Factor eIFiso4G Is Required to Regulate Violaxanthin De-epoxidase Expression in *Arabidopsis***

May 16, 2014 The Journal of Biological Chemistry, 289, 13926-13936.

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The eukaryotic translation initiation factor (eIF) 4G is a scaffold protein that organizes the assembly of those initiation factors needed to recruit the 40 S ribosomal subunit to an mRNA. Plants, like many eukaryotes, express two eIF4G isoforms. eIFiso4G, one of the isoforms specific to plants, is unique among eukaryotic eIF4G proteins in that it is highly divergent and unusually small in size, raising the possibility of functional specialization. In this study, the role of eIFiso4G in plant growth was investigated using null mutants for the eIF4G isoforms in *Arabidopsis*. eIFiso4G loss of function mutants exhibited smaller cell, leaf, plant size, and biomass accumulation that correlated with its reduced photosynthetic activity, phenotypes not observed with the eIF4G loss of function mutant.

Although no change in photorespiration or dark respiration was observed in the eIFiso4G loss of function mutant, a reduction in chlorophyll levels and an increase in the level of nonphotochemical quenching were observed. An increase in xanthophyll cycle activity and the generation of reactive oxygen species contributed to the qE and qI components of non-photochemical quenching, respectively. An increase in the transcript and protein levels of violaxanthin de-epoxidase in the eIFiso4G loss of function mutant and an increase in its xanthophyll de-epoxidation state correlated with the higher qE associated with loss of eIFiso4G expression. These observations indicate that eIFiso4G expression is required to regulate violaxanthin de-epoxidase expression and to support photosynthetic activity.

### Angela:

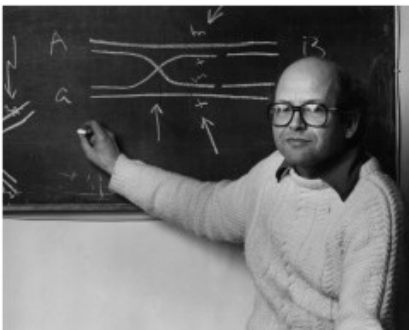
#### 1) Molecular Cell

Obituary

Robin Holliday 1932–2014

Founder of the field of genetic recombination.

<http://dx.doi.org/10.1016/j.molcel.2014.05.010>



Robin Holliday



Bronze sculpture

#### 2) **A Novel ER Stress-Independent Function of the UPR in Angiogenesis**

Hery Urra, Claudio Hetz

Tumors rely on the unfolded protein response (UPR) and angiogenesis to survive the metabolic stress of hypoxia. Karali et al. (2014) revealed that VEGF signaling engages UPR sensors in an unconventional manner that is independent of endoplasmic reticulum (ER) stress, mediated by mTOR signaling to promote endothelial cell survival and angiogenesis.

<http://dx.doi.org/10.1016/j.molcel.2014.05.013>

### 3) Mitotic Wnt Signaling Promotes Protein Stabilization and Regulates Cell Size

Sergio P. Acebron, Emil Karaulanov, Birgit S. Berger, Ya-Lin Huang, Christof Niehrs

Wnt signaling is thought to regulate cell behavior mainly by transcription of target genes. Acebron et al. show that Wnt signaling slows down protein degradation as cells prepare to divide. This Wnt-dependent stabilization of proteins (Wnt/STOP) is independent of transcription and increases cell size.

<http://dx.doi.org/10.1016/j.molcel.2014.04.014>

BMC

The past twenty years or so have seen a revolution in the perception of mitochondria, from the discrete bioenergetic organelles of 20<sup>th</sup>-century textbooks to a network undergoing constant fission and fusion regulated by cellular needs and physiological state, engaging with other membrane systems, and signalling to the machinery of the cytoplasm the metabolic status of the cell.

**Editorial by Miranda Robertson**

<http://www.biomedcentral.com/1741-7007/12/37>

### 4) Review

## Mitochondria as signaling organelles

**Navdeep S Chandel**

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Almost 20 years ago, the discovery that mitochondrial release of cytochrome c initiates a cascade that leads to cell death brought about a wholesale change in how cell biologists think of mitochondria. Formerly viewed as sites of biosynthesis and bioenergy production, these double membrane organelles could now be thought of as regulators of signal transduction. Within a few years, multiple other mitochondria-centric signaling mechanisms have been proposed, including release of reactive oxygen species and the scaffolding of signaling complexes on the outer mitochondrial membrane. It has also been shown that mitochondrial dysfunction causes induction of stress responses, bolstering the idea that mitochondria communicate their fitness to the rest of the cell. In the past decade, multiple new modes of mitochondrial signaling have been discovered. These include the release of metabolites, mitochondrial motility and dynamics, and interaction with other organelles such as endoplasmic reticulum in regulating signaling. Collectively these studies have established that mitochondria-dependent signaling has diverse physiological and pathophysiological outcomes. This review is a brief account of recent work in mitochondria-dependent signaling in the historical framework of the early studies.

