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## **Self-clearance mechanism of mitochondrial E3 ligase MARCH5 contributes to mitochondria quality control**

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MARCH5, a mitochondrial E3 ubiquitin ligase, controls mitochondrial dynamics proteins and misfolded proteins, and has been proposed to play a role in mitochondria quality control. However, it remains unclear how mutant MARCH5 found in cancer tissues is removed from cells. Here, we show that mutation in the MARCH5 ligase domain increased its half-life fourfold, resulting in a drastic increase in its protein level. Abnormal accumulation of the E3 ligase-defective MARCH5 mutants MARCH5<sup>H43W</sup> and MARCH5<sup>C65/68S</sup> was diminished by overexpression of active MARCH5<sup>WT</sup>; the mutant proteins were degraded through the ubiquitin–proteasome pathway. Coimmunoprecipitation revealed that MARCH5 forms homodimers, and that substitution of Gly to Leu at the first putative GxxxG dimerization motif, but not the second, resulted in a loss of dimeric interaction. Moreover, overexpression of the dimerization-defective mutant MARCH5<sup>4GL</sup> could not decrease the level of accumulated MARCH5<sup>H43W</sup>, suggesting that dimerization of MARCH5 is necessary for self-clearance. Abnormal accumulation of MARCH5<sup>H43W</sup> and mitochondrial hyperfusion led to NF-κB activation, which was suppressed by overexpression of MARCH5<sup>WT</sup>. Together, the data reveal a self-protective mechanism involving MARCH5, which can target its own dysfunctional mutant for degradation in order to maintain mitochondrial homeostasis.

Minsoo

### **1. Artificial remodelling of alternative electron flow by flavodiiron proteins in Arabidopsis**

Hiroshi Yamamoto, Shunichi Takahashi, Murray R. Badger & Toshiharu Shikanai  
Nature Plants Article number: 16012 (2016)

22 February 2016

Abstract

In photosynthesis, linear electron transport from water to nicotinamide adenine dinucleotide phosphate (NADP<sup>+</sup>) cannot satisfy the ATP/NADPH production stoichiometry required by the Calvin–Benson cycle. Cyclic electron transport (CET) around photosystem I (PSI) and pseudocyclic electron transport (pseudoCET) can produce ATP without the accumulation of NADPH. Flavodiiron proteins (Flv) are the main mediator of pseudoCET in photosynthetic organisms, spanning cyanobacteria to gymnosperms. However, their genes are not conserved in angiosperms. Here we explore the possibility of complementing CET with Flv-dependent pseudoCET in the angiosperm *Arabidopsis thaliana*. We introduced FlvA and FlvB genes from the moss *Physcomitrella patens* into both wild-type (WT) *Arabidopsis* and the proton gradient regulation 5 (*pgr5*) mutant, which is defective in the main pathway of CET.

We measured rates of pseudoCET using membrane inlet mass spectrometry, along with several photosynthetic parameters. Flv expression significantly increased rates of pseudoCET in the mutant plants, particularly at high light intensities, and partially restored the photosynthetic phenotype. In WT plants, Flv did not compete with PGR5-dependent CET during steady-state photosynthesis, but did form a large electron sink in fluctuating light. We conclude that flavodiiron proteins can help to protect the photosystems in Arabidopsis under fluctuating light, even in the presence of CET.

2. Mol Cell. 2016 Feb 18;61(4):614-24. doi: 10.1016/j.molcel.2016.01.010. Epub 2016

Feb 11.

### **Deubiquitination and Activation of AMPK by USP10.**

Deng M(1), Yang X(2), Qin B(3), Liu T(1), Zhang H(1), Guo W(4), Lee SB(1), Kim JJ(1), Yuan J(5), Pei H(2), Wang L(6), Lou Z(7).

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The AMP-activated protein kinase (AMPK) is the master regulator of metabolic homeostasis by sensing cellular energy status. When intracellular ATP levels decrease during energy stress, AMPK is initially activated through AMP or ADP binding and phosphorylation of a threonine residue (Thr-172) within the activation loop of its kinase domain. Here we report a key molecular mechanism by which AMPK activation is amplified under energy stress. We found that ubiquitination on AMPK $\alpha$  blocks AMPK $\alpha$  phosphorylation by LKB1. The deubiquitinase

USP10 specifically removes ubiquitination on AMPK $\alpha$  to facilitate AMPK $\alpha$  phosphorylation by LKB1. Under energy stress, USP10 activity in turn is enhanced through AMPK-mediated phosphorylation of Ser76 of USP10. Thus, USP10 and AMPK

form a key feedforward loop ensuring amplification of AMPK activation in response to fluctuation of cellular energy status. Disruption of this feedforward loop leads to improper AMPK activation and multiple metabolic defects.

3. Mol Cell. 2016 Feb 18;61(4):625-39. doi: 10.1016/j.molcel.2016.01.013. Epub 2016 Feb 11.

**mTORC1 Coordinates Protein Synthesis and Immunoproteasome Formation via PRAS40 to Prevent Accumulation of Protein Stress.**

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Reduction of translational fidelity often occurs in cells with high rates of protein synthesis, generating defective ribosomal products. If not removed, such aberrant proteins can be a major source of cellular stress causing human diseases. Here, we demonstrate that mTORC1 promotes the formation of immunoproteasomes for efficient turnover of defective proteins and cell survival. mTORC1 sequesters precursors of immunoproteasome  $\beta$  subunits via PRAS40.

When

activated, mTORC1 phosphorylates PRAS40 to enhance protein synthesis and simultaneously to facilitate the assembly of the  $\beta$  subunits for forming immunoproteasomes. Consequently, the PRAS40 phosphorylations play crucial roles

in clearing aberrant proteins that accumulate due to mTORC1 activation. Mutations of RAS, PTEN, and TSC1, which cause mTORC1 hyperactivation, enhance immunoproteasome formation in cells and tissues. Those mutations increase cellular dependence on immunoproteasomes for stress response and survival.

These

results define a mechanism by which mTORC1 couples elevated protein synthesis with immunoproteasome biogenesis to protect cells against p

Jarett

Zhou, Y., et al. "Cloning and characterization of filamentous fungal S-nitrosoglutathione reductase from *Aspergillus nidulans*." *Journal of microbiology and biotechnology* (2016).

Schippers, Jos HM, Christine H. Foyer, and Joost T. van Dongen. "Redox regulation in shoot growth, SAM maintenance and flowering." *Current Opinion in Plant Biology* 29 (2016): 121-128.

Damian

**Nitric oxide function in plant abiotic stress** Nurun Nahar Fancy, Ann-Kathrin Bahlmann and Gary J. Loake  
EST | DOI: 10.1111/pce.12707

Accepted manuscript

In this manuscript, we focus on the current state-of-the-art regarding the role of nitric oxide (NO) and significant because NO and S-nitrosylation are emerging as important players in plant abiotic stress signaling. This article is protected by copyright, for all rights reserved. plant abiotic stress, signalling, redox regulation, NO function and S-nitrosylation. This article is protected

Archives of Biochemistry and Biophysics: Alert 16 January-22 January  
**Structural changes upon peroxynitrite-mediated nitration of peroxiredoxin 2; nitrated Prx2 resembles its disulfide-oxidized form** Pages 101-108 Lía Randall, Bruno Manta, Kimberly J. Nelson, Javier Santos, Leslie B. Poole, Ana Denicola

Peroxiredoxins are cys-based peroxidases that function in peroxide detoxification and H<sub>2</sub>O<sub>2</sub>-induced signaling. Human Prx2 is a typical 2-Cys Prx arranged as pentamers of head-to-tail homodimers. During the catalytic mechanism, the active-site cysteine (C<sub>P</sub>) cycles between reduced, sulfenic and disulfide state involving conformational as well as oligomeric changes. Several post-translational modifications were shown to affect Prx activity, in particular C<sub>P</sub> overoxidation which leads to inactivation. We have recently reported that nitration of Prx2, a post-translational modification on non-catalytic tyrosines, unexpectedly increases its peroxidase activity and resistance to overoxidation. To elucidate the cross-talk between this post-translational modification and the enzyme catalysis, we investigated the structural changes of Prx2 after nitration. Analytical ultracentrifugation, UV absorption, circular dichroism, steady-state and time-resolved fluorescence were used to connect catalytically relevant redox changes with tyrosine nitration. Our results show that the reduced nitrated Prx2 structurally resembles the disulfide-oxidized native form of the enzyme favoring a locally unfolded conformation that facilitates

disulfide formation. These results provide structural basis for the kinetic analysis previously reported, the observed increase in activity and the resistance to overoxidation of the peroxynitrite-treated enzyme.

Nitrosylation of RyR2 Prevents Activation of Ca Waves Induced by Redox-Mediated Intersubunit Cross-Linking

Cited in Scopus: 0

Elisa Bovo, Stefan R. Mazurek, Jody L. Martin, Pieter P. de Tombe, Aleksey V. Zima  
Biophysical Journal, Vol. 110, Issue 3, p270a  
Published in issue: February 16, 2016

We have recently discovered a novel post-translational modification of type-2 ryanodine receptor (cardiac RyR2) induced by oxidative stress: intersubunit cross-linking (XL). Because RyR gating is associated with large-scale intersubunit dynamics, we hypothesized that XL is functionally the most important redox

modification of RyR2. We have developed a simple cell model system to define the functional importance of RyR2 XL. We found that co-expressing recombinant human RyR2 and the SR Ca-ATPase (SERCA2a) in HEK293 cells generates Ca oscillations with similar kinetics to cardiac Ca waves.

[Peroxynitrite Produced via Nitric Oxide Synthesis in Isolated Cardiac Mitochondria](#)

Cited in Scopus: 0

Harrison J. Gerdes, Amadou K.S. Camara, James S. Heisner, David F. Stowe

Biophysical Journal, Vol. 110, Issue 3, p475a

Published in issue: February 16, 2016

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It is controversial whether or not isolated mitochondria contain an endogenous nitric oxide synthase (NOS). NOS catalyzes the production of the gaseous signaling molecule NO•(nitric oxide). During ischemia/reperfusion (IR) injury, NO•reacts with superoxide (O<sub>2</sub>•<sup>-</sup>) to form the oxidant peroxynitrite (ONOO<sup>-</sup>), which can cause tissue damage and initiate deleterious post-translational modifications of cellular proteins. The aim of this project is to detect the production of ONOO<sup>-</sup> in isolated mitochondria under conditions of oxidative/nitrosative stress, and to determine whether the ONOO<sup>-</sup> production is dependent on the presence of endogenous mitochondrial NOS.

Precise Control and Measurement of Temperature with Femtosecond Optical Tweezers

Cited in Scopus: 0

Dipankar Mondal, Debabrata Goswami  
Biophysical Journal, Vol. 110, Issue 3, p500a  
Published in issue: February 16, 2016

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Optical traps have often been used for physical manipulation and transport within liquids for studying bio-systems. In this connection, though a lot of work has focused on the property of the trapped particle, there is little effort on utilizing the effect of the trapping environment. Here we demonstrate a novel method for exploiting the effect of trapping environment in observing the temperature rise in liquids directly at the vicinity of an optical trap center. Our approach utilizes the photo-thermal effect at micro-volume dimension to measure temperature, which could eventually be extended to *in-vivo* conditions.

Overcoming Heterogeneity to Study the Structure and Assembly of Small Heat-Shock Protein Chaperones with Non-Aggregating Clients

Cited in Scopus: 0

Miranda Collier, Justin Benesch  
Biophysical Journal, Vol. 110, Issue 3, p368a  
Published in issue: February 16, 2016

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The small heat-shock proteins (sHSPs) are a family of molecular chaperones that act as a first line of defence in stress response to prevent irreversible aggregation of denaturing proteins in the cell. Most sHSPs form large oligomeric ensembles, often adopting multiple interconverting stoichiometries and architectures. This heterogeneity presents a challenge for many biophysical techniques. Native mass spectrometry (MS) is a useful method for characterising noncovalent protein assemblies, and has been applied to the sHSPs to identify oligomeric states.

Intrinsically-Disordered Region of Human Small Heat Shock Protein HSPB1 Affects Structure and Function

Amanda F. Clouser, Ponni Rajagopal, Rachel E. Klevit

Biophysical Journal, Vol. 110, Issue 3, p43a

Published in issue: February 16, 2016

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Found in all kingdoms of life, small heat shock proteins (sHSPs) are molecular chaperones whose primary function is to maintain aggregation-prone proteins in a soluble state. Most mammalian sHSPs exist as highly dynamic, polydisperse oligomers. The basic structural unit is a dimer formed via a conserved central  $\alpha$ -crystallin domain. The highly divergent N-terminal domain (NTD) is responsible for the diverse and unique oligomerization properties of sHSPs. NTDs are predicted to be disordered and are highly hydrophobic, making them intractable structural targets individually.

Indu

### **1.Plant scientists: GM technology is safe**

BY NOAH FAHLGREN, REBECCA BART, LUIS HERRERA-ESTRELLA, RUBÉN RELLÁN-ÁLVAREZ, DANIEL H. CHITWOOD, JOSÉ R. DINNENY  
SCIENCE19 FEB 2016 : 824

### **2. Calling all failed replication experiments**

BY JOCELYN KAISER

SCIENCE05 FEB 2016 : 548

### **3.Structures of a CRISPR-Cas9 R-loop complex primed for DNA cleavage**

Fuguo Jiang<sup>1,\*</sup>, David W. Taylor<sup>1,2,\*</sup>, Janice S. Chen<sup>1</sup>, Jack E. Kornfeld<sup>3</sup>, Kaihong Zhou<sup>3</sup>, Aubri J. Thompson<sup>4</sup>, Eva Nogales<sup>1,2,3,5,†</sup>, Jennifer A. Doudna<sup>1,2,3,4,5,†</sup>  
*Science* 19 Feb 2016:Vol. 351, Issue 6275, pp. 867-871

### **4.RPN1 PROVIDES ADJACENT RECEPTOR SITES FOR SUBSTRATE BINDING AND DEUBIQUITINATION BY THE PROTEASOME**

Yuan Shi<sup>1,\*</sup>, Xiang Chen<sup>2,\*</sup>, Suzanne Elsassner<sup>1,\*</sup>, Bradley B. Stocks<sup>3,\*</sup>, Geng Tian<sup>1</sup>, Byung-Hoon Lee<sup>1</sup>, Yanhong Shi<sup>2,4</sup>, Naixia Zhang<sup>4</sup>, Stefanie A. H. de Poot<sup>1</sup>, Fabian Tuebing<sup>1</sup>, Shuangwu Sun<sup>1</sup>, Jacob Vannoy<sup>2, 5</sup>, Sergey G. Tarasov<sup>6</sup>, John R. Engen<sup>3,†</sup>, Daniel Finley<sup>1,†</sup>, Kylie J. Walters  
*Science* 19 Feb 2016:Vol. 351, Issue 6275, pp.

### **5.Using decoys to expand the recognition specificity of a plant disease resistance protein**

Sang Hee Kim<sup>\*</sup>, Dong Qi<sup>†</sup>, Tom Ashfield, Matthew Helm, Roger W. Innes<sup>‡</sup>  
*Science* 12 Feb 2016: Vol. 351, Issue 6274, pp. 684-687

Keith

**Plasmodium falciparum Hsp70-z, an Hsp110 homologue, exhibits independent chaperone activity and interacts with Hsp70-1 in a nucleotide-dependent fashion.**

Cell Stress Chaperones. 2016 Feb 19.

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The role of molecular chaperones, among them heat shock proteins (Hsps), in the development of malaria parasites has been well documented. Hsp70s are molecular chaperones that facilitate protein folding. Hsp70 proteins are composed of an N-terminal nucleotide binding domain (NBD), which confers them with ATPase activity and a C-terminal substrate binding domain (SBD). In the ADP-bound state, Hsp70 possesses high affinity for substrate and releases the folded substrate when it is bound to ATP. The two domains are connected by a conserved linker segment. Hsp110 proteins possess an extended lid segment, a feature that distinguishes them from canonical Hsp70s. *Plasmodium falciparum* Hsp70-z (PfHsp70-z) is a member of the Hsp110 family of Hsp70-like proteins. PfHsp70-z is essential for survival of malaria parasites and is thought to play an important role as a molecular chaperone and nucleotide exchange factor of its cytosolic canonical Hsp70 counterpart, PfHsp70-1. Unlike PfHsp70-1 whose functions are fairly well established, the structure-function features of PfHsp70-z remain to be fully elucidated. In the current study, we established that PfHsp70-z possesses independent chaperone activity. In fact, PfHsp70-z appears to be marginally more effective in suppressing protein aggregation than its cytosol-localized partner, PfHsp70-1. Furthermore, based on coimmunoaffinity chromatography and surface plasmon resonance analyses, PfHsp70-z associated with PfHsp70-1 in a nucleotide-dependent fashion. Our findings suggest that besides serving as a molecular chaperone, PfHsp70-z could facilitate the nucleotide exchange function of PfHsp70-1. These dual functions explain why it is essential for parasite survival.

## **The genome of the seagrass *Zostera marina* reveals angiosperm adaptation to the sea**

Jeanine L. Olsen, Pierre Rouzé, Bram Verhelst, Yao-Cheng Lin, Till Bayer, Jonas Collen, Emanuela Dattolo, Emanuele De Paoli, Simon Dittami, Florian Maumus, Gurvan Michel, Anna Kersting, Chiara Lauritano, Rolf Lohaus, Mats Töpel, Thierry Tonon, Kevin Vanneste, Mojgan Amirebrahimi, Janina Brakel, Christoffer Boström, Mansi Chovatia, Jane Grimwood, Jerry W. Jenkins, Alexander Jueterbock, Amy Mraz, Wytze T. Stam, Hope Tice, Erich Bornberg-Bauer, Pamela J. Green, Gareth A. Pearson, Gabriele Procaccini, Carlos M. Duarte, Jeremy Schmutz, Thorsten B. H. Reusch & Yves Van de Peer

*Nature* **530**, 331–335 (18 February 2016)

Seagrasses colonized the sea<sup>1</sup> on at least three independent occasions to form the basis of one of the most productive and widespread coastal ecosystems on the planet<sup>2</sup>. Here we report the genome of *Zostera marina* (L.), the first, to our knowledge, marine angiosperm to be fully sequenced. This reveals unique insights into the genomic losses and gains involved in achieving the structural and physiological adaptations required for its marine lifestyle, arguably the most severe habitat shift ever accomplished by flowering plants. Key angiosperm innovations that were lost include the entire repertoire of stomatal genes<sup>3</sup>, genes involved in the synthesis of terpenoids and ethylene signalling, and genes for ultraviolet protection and phytochromes for far-red sensing. Seagrasses have also regained functions enabling them to adjust to full salinity. Their cell walls contain all of the polysaccharides typical of land plants, but also contain polyanionic, low-methylated pectins and sulfated galactans, a feature shared with the cell walls of all macroalgae<sup>4</sup> and that is important for ion homeostasis, nutrient uptake and O<sub>2</sub>/CO<sub>2</sub> exchange through leaf epidermal cells. The *Z. marina* genome resource will markedly advance a wide range of functional ecological studies from adaptation of marine ecosystems under climate warming<sup>5,6</sup>, to unravelling the mechanisms of osmoregulation under high salinities that may further inform our understanding of the evolution of salt tolerance in crop plants<sup>7</sup>.