

Keith Ballard:

## **Atomic structure of Hsp90-Cdc37-Cdk4 reveals that Hsp90 traps and stabilizes an unfolded kinase**

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The Hsp90 molecular chaperone and its Cdc37 cochaperone help stabilize and activate more than half of the human kinome. However, both the mechanism by which these chaperones assist their "client" kinases and the reason why some kinases are addicted to Hsp90 while closely related family members are independent are unknown. Our structural understanding of these interactions is lacking, as no full-length structures of human Hsp90, Cdc37, or either of these proteins with a kinase have been elucidated. Here we report a 3.9 angstrom cryo-electron microscopy structure of the Hsp90-Cdc37-Cdk4 kinase complex. Surprisingly, the two lobes of Cdk4 are completely separated with the  $\beta$ 4- $\beta$ 5 sheet unfolded. Cdc37 mimics part of the kinase N lobe, stabilizing an open kinase conformation by wedging itself between the two lobes. Finally, Hsp90 clamps around the unfolded kinase  $\beta$ 5 strand and interacts with exposed N- and C-lobe interfaces, protecting the kinase in a trapped unfolded state. On the basis of this structure and an extensive amount of previously collected data, we propose unifying conceptual and mechanistic models of chaperone-kinase interactions.

## **In Vivo Conformational Dynamics of Hsp90 and Its Interactors**

Cell Chem Biol. 2016 Jun 23;23(6):716-26.

Chavez JD1, Schweppe DK1, Eng JK1, Bruce JE2.

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Hsp90 belongs to a family of some of the most highly expressed heat shock proteins that function as molecular chaperones to protect the proteome not only from the heat shock but also from other misfolding events. As many client proteins of Hsp90 are involved in oncogenesis, this chaperone has been the focus of intense research efforts. Yet, we lack structural information for how Hsp90 interacts with co-chaperones and client proteins. Here, we developed a mass-spectrometry-based approach that allowed quantitative measurements of in vitro and in vivo effects of small-molecule inhibitors on Hsp90 conformation, and interaction with co-

chaperones and client proteins. From this analysis, we were able to derive structural models for how Hsp90 engages its interaction partners in vivo, and how different drugs affect these structures. In addition, the methodology described here offers a new approach to probe the effects of virtually any inhibitor treatment on the proteome level.

### **Intracellular formation of $\alpha$ -synuclein oligomers and the effect of heat shock protein 70 characterized by confocal single particle spectroscopy**

Biochem Biophys Res Commun. 2016 Jun 7.

Levin J1, Hillmer AS2, Högen T3, McLean PJ4, Giese A5.

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2Center for Neuropathology and Prion Research, Ludwig-Maximilians-University, Feodor-Lynen-Str. 23, 81377 Munich, Germany.

3Department of Neurology, Ludwig-Maximilians-University, Marchioninstr. 15, 81377 Munich, Germany.

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5Center for Neuropathology and Prion Research, Ludwig-Maximilians-University, Feodor-Lynen-Str. 23, 81377 Munich, Germany.

Synucleinopathies such as dementia with Lewy bodies or Parkinson's disease are characterized by intracellular deposition of pathologically aggregated  $\alpha$ -synuclein. The details of the molecular pathogenesis of PD and especially the conditions that lead to intracellular aggregation of  $\alpha$ -synuclein and the role of these aggregates in cell death remain unknown. In cell free in vitro systems considerable knowledge about the aggregation processes has been gathered. In comparison, the knowledge about these aggregation processes in cells is far behind. In cells  $\alpha$ -synuclein aggregates can be toxic. However, the crucial particle species responsible for decisive steps in pathogenesis such as seeding a continuing aggregation process and triggering cell death remain to be identified. In order to understand the complex nature of intracellular  $\alpha$ -synuclein aggregate formation, we analyzed fluorescent particles formed by venus and  $\alpha$ -synuclein-venus fusion proteins and  $\alpha$ -synuclein-hemi-venus fusion proteins derived from gently lysed cells. With these techniques we were able to identify and characterize  $\alpha$ -synuclein oligomers formed in cells. Especially the use of  $\alpha$ -synuclein-hemi-venus fusion proteins enabled us to identify very small  $\alpha$ -synuclein oligomers with high sensitivity. Furthermore, we were able to study the molecular effect of heat shock protein 70, which is known to inhibit  $\alpha$ -synuclein aggregation in cells. Heat shock protein 70 does not only influence the size of  $\alpha$ -synuclein oligomers, but also their quantity. In summary, this approach based on fluorescence single particle spectroscopy, that is suited for high throughput measurements, can be used to detect and characterize intracellularly formed  $\alpha$ -synuclein aggregates and characterize the effect of molecules that interfere with  $\alpha$ -synuclein aggregate formation.

### **Anti-aggregation activity of small heat shock proteins under crowded conditions**

Int J Biol Macromol. 2016 May 24

Roman SG1, Chebotareva NA2, Kurganov BI2

1&2Bach Institute of Biochemistry, Research Center of Biotechnology of the Russian Academy of Sciences, Leninsky pr. 33, Moscow 119071, Russia.

It is becoming evident that small heat shock proteins (sHsps) are important players of protein homeostasis system. Their ability to bind misfolded proteins may play a crucial role in preventing protein aggregation in cells. The remarkable structural plasticity of sHsps is considered to underlie the mechanism of their activity. However, all our knowledge of the anti-aggregation functioning of sHsps is based on data obtained in vitro in media greatly different from the cellular highly crowded milieu. The present review highlights available data on the effect of crowding on the anti-aggregation activity of sHsps. There is some evidence that crowding affects conformation and dynamics of sHsps oligomers as well as their anti-aggregation properties. Crowding stimulates association of sHsp-client protein complexes into large-sized aggregates thus diminishing the apparent anti-aggregation activity of sHsps. Nevertheless, it is also shown that complexes between suboligomers (dissociated forms) of sHsps and client proteins may be stabilized and exist for longer period of time under crowded conditions. Moreover, crowding may retard the initial stages of aggregation which correspond to the formation of sHsp-containing nuclei and their clusters. Thus, dissociation of sHsps into suboligomers appears to be an important feature for the anti-aggregation activity of sHsps in crowded media.

### **sHSPdb: a database for the analysis of small Heat Shock Proteins**

BMC Plant Biol. 2016 Jun 13;16(1):135.

Jaspard E1,2,3, Hunault G4

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2INRA, UMR 1345 IRHS, Beaucouzé, France. emmanuel.jaspard@univ-angers.fr.

3Agrocampus-Ouest, UMR 1345 IRHS, Angers, France. emmanuel.jaspard@univ-angers.fr.

4Université d'Angers, Laboratoire d'Hémodynamique, Interaction Fibrose et Invasivité tumorale hépatique, UPRES 3859, IFR 132, F-49045, Angers, France.

### **BACKGROUND:**

small Heat Shock Proteins (sHSP) is a wide proteins family. SHSP are found in all kingdoms and they play critical roles in plant stress tolerance mechanisms (as well as in pathogenic microorganisms and are implicated in human diseases).

### **RESULTS:**

sHSPdb (small Heat Shock Proteins database) is an integrated resource containing non-redundant, full-length and curated sequences of sHSP, classified on the basis of amino acids motifs and physico-chemical

properties. sHSPdb gathers data about sHSP defined by various databases (Uniprot, PFAM, CDD, InterPro). It provides a browser interface for retrieving information from the whole database and a search interface using various criteria for retrieving a refined subset of entries. Physicochemical properties, amino acid composition and combinations are calculated for each entry. sHSPdb provides automatic statistical analysis of all sHSP properties. Among various possibilities, sHSPdb allows BLAST searches, alignment of selected sequences and submission of sequences.

## **CONCLUSIONS:**

sHSPdb is a new database containing information about sHSP from all kingdoms. sHSPdb provides a classification of sHSP, as well as tools and data for the analysis of the structure - function relationships of sHSP. Data are mainly related to various physico-chemical properties of the amino acids sequences of sHSP. sHSPdb is accessible at <http://forge.info.univ-angers.fr/~gh/Shspdb/index.php> .

## **Damian Guerra:**

Kuruthukulangarakoola GT, Zhang J, Albert A, Winkler B, Lang H, Buegger F, Gaupels F, Heller W, Michalke B, Sarioglu H, Schnitzler JP, Hebelstrup KH, Durner J, Lindermayr C.

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Plant Cell Rep. 2016 Jun 13;. [ PMID: 27294277 [PubMed - as supplied by publisher]

Expression of alcohol dehydrogenase 5 in ovarian carcinoma: Effect on prognosis and therapeutic potential S.

Sakra , S. Girib , R. Rattanb , E. Abdulfataha , V. Pardeshic , R.T. Morrissa , A.R. Munkarahb , R. Ali-Fehmia .  
a Wayne State University School of Medicine, Detroit, MI, USA, b Henry Ford Health System, Detroit, MI, USA, c Karmanos Cancer Center, Wayne State University, Detroit, MI, USA

## **Featured Poster Session**

He W, Frost MC. Direct measurement of actual levels of nitric oxide (NO) in cell culture conditions using soluble NO donors. Redox Biology. 2016;9:1-14.

## **Prof. Vierling:**

O'Meara TR, Veri AO, Polvi EJ, Li X, Valaei SF, Diezmann S, Cowen LE.

Mapping the Hsp90 Genetic Network Reveals Ergosterol Biosynthesis and Phosphatidylinositol-4-Kinase Signaling as Core Circuitry Governing Cellular Stress.

PLoS Genet. 2016 Jun;12(6):e1006142. PMID: 27341673 [PubMed - as supplied by publisher]

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[Volume 157, Issue 3 Pages 255 - 399, July 2016](#)

Special Issue: Plant Mitochondria

**What is hot in plant mitochondria? (pages 256–263)**

Ian Max Møller Version of Record online: 1 JUN 2016 | DOI: 10.1111/ppl.12456

**Refined method to study the posttranslational regulation of alternative oxidases from *Arabidopsis thaliana* in vitro (pages 264–279)**

Jennifer Selinski, Andreas Hartmann, Saskia Höfler, Gabriele Deckers-Hebestreit and Renate Scheibe

Version of Record online: 16 MAR 2016 | DOI: 10.1111/ppl.12418

**Maturation of 5' ends of plant mitochondrial RNAs (pages 280–288)**

Stefan Binder, Katrin Stoll and Birgit Stoll

Version of Record online: 23 MAR 2016 | DOI: 10.1111/ppl.12423

**The carbonic anhydrase domain of plant mitochondrial complex I (pages 289–296)**

Steffanie Fromm, Jennifer Senkler, Eduardo Zabaleta, Christoph Peterhänsel and Hans-Peter Braun

Version of Record online: 5 APR 2016 | DOI: 10.1111/ppl.12424

**Definition of a core module for the nuclear retrograde response to altered organellar gene expression identifies GLK overexpressors as *gun* mutants (pages 297–309)**

Dario Leister and Tatjana Kleine

Version of Record online: 4 APR 2016 | DOI: 10.1111/ppl.12431

**Cytochrome *c*, a hub linking energy, redox, stress and signaling pathways in mitochondria and other cell compartments (pages 310–321)**

Elina Welchen and Daniel H. Gonzalez

Version of Record online: 23 MAY 2016 | DOI: 10.1111/ppl.12449

**Alternative oxidase: a respiratory electron transport chain pathway essential for maintaining photosynthetic performance during drought stress (pages 322–337)**

Greg C. Vanlerberghe, Greg D. Martyn and Keshav Dahal

Version of Record online: 24 MAY 2016 | DOI: 10.1111/ppl.12451

**The evolution of substrate specificity-associated residues and Ca<sup>2+</sup>-binding motifs in EF-hand-containing type II NAD(P)H dehydrogenases (pages 338–351)**

Meng-Shu Hao and Allan G. Rasmusson

Version of Record online: 30 MAY 2016 | DOI: 10.1111/ppl.12453

**Dealing with the sulfur part of cysteine: four enzymatic steps degrade l-cysteine to pyruvate and thiosulfate in *Arabidopsis* mitochondria (pages 352–366)**

Saskia Höfler, Christin Lorenz, Tjorven Busch, Mascha Brinkkötter, Takayuki Tohge, Alisdair R. Fernie, Hans-Peter Braun and Tatjana M. Hildebrandt

Version of Record online: 3 JUN 2016 | DOI: 10.1111/ppl.12454

**The origin of cytosolic ATP in photosynthetic cells (pages 367–379)**

Per Gardeström and Abir U. Igamberdiev

Version of Record online: 26 MAY 2016 | DOI: 10.1111/ppl.12455

**Divergent evolution of the M3A family of metallopeptidases in plants (pages 380–388)**

Beata Kmiec, Pedro F. Teixeira, Monika W. Mucha and Elzbieta Glaser

Version of Record online: 3 JUN 2016 | DOI: 10.1111/ppl.12457

## **The roles of mitochondrial transcription termination factors (MTERFs) in plants (pages 389–399)**

Víctor Quesada

Version of Record online: 14 MAR 2016 | DOI: 10.1111/ppl.12416

Cellular Signalling: Alert 15 June-21 June

[Bridges between mitochondrial oxidative stress, ER stress and mTOR signaling in pancreatic  \$\beta\$  cells](#) Review Article

Pages 1099-1104

Jing Wang, Xin Yang, Jingjing Zhang

[Phosphorylated heat shock protein 27 promotes lipid clearance in hepatic cells through interacting with STAT3 and activating autophagy](#) Original Research Article

Pages 1086-1098

Lei Shen, Zhilin Qi, Yanyan Zhu, Xiaomeng Song, Chunxia Xuan, Peiling Ben, Lei Lan, Lan Luo, Zhimin Yin

Nature Microbiology - Table of Contents alert, Volume 1, July 2016

Review Article | 24 June 2016

## **Drug resistance in eukaryotic microorganisms**

Alan H. Fairlamb, Neil A. R. Gow, Keith R. Matthews & Andrew P. Waters

*Nature Microbiology* **1**, Article number: 16092 | doi:10.1038/nmicrobiol.2016.92

## **Making error-free DNA from RNA**

DNA polymerase enzymes copy DNA into new strands of identical DNA. Reverse transcriptase (RT) enzymes copy RNA into DNA. Unlike many DNA polymerases, RT enzymes do not have a proofreading function that checks for errors in the newly synthesized DNA. Ellefson *et al.* use in vitro directed evolution and protein engineering to build an error-correcting RT from a prokaryotic DNA polymerase. The RT “xenopolymerase” shows increased fidelity as compared to natural RTs and should streamline and increase the precision of transcriptomics methods.

*Science*, this issue p. [1590](#)

Plant Journal

## **IRE1, a component of the Unfolded Protein Response signaling pathway, protects pollen development in Arabidopsis from heat stress**

Yan Deng, Renu Srivastava, Teagen D. Quilichini, Haili Dong, Yan Bao, Harry T. Horner and Stephen H. Howell

Accepted manuscript online: 15 JUN 2016 10:21AM EST | DOI: 10.1111/tpj.13239

Wu X, Jiang L, Yu M, An X, Ma R, Yu Z.

Proteomic analysis of changes in mitochondrial protein expression during peach fruit ripening and senescence.

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Rivera-Contreras IK, Zamora-Hernández T, Huerta-Heredia AA, Capataz-Tafur J, Barrera-Figueroa BE, Juntawong P, Peña-Castro JM.  
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tRNA-related sequences trigger systemic mRNA transport in plants  
Wenna Zhang, Christoph Thieme, Gregor Kollwig, Federico Apelt, Lei Yang, Winter Winter, Nadine Andresen, Dirk Walther, and Friedrich Kragler

Plant Cell 2016 tpc.15.01056; Advance Publication June 7, 2016; doi:10.1105/tpc.15.01056 **OPEN**  
<http://www.plantcell.org/content/early/2016/06/07/tpc.15.01056.abstract>

In plants, protein-coding messenger RNAs (mRNAs) can move via the phloem vasculature to distant tissues, where they may act as non-cell-autonomous signals. Emerging work has identified many phloem-mobile mRNAs, but little is known regarding RNA motifs triggering mobility, the extent of mRNA transport, and the potential of transported mRNAs to be translated into functional proteins after transport. To address these aspects, we produced reporter transcripts harboring transfer RNA (tRNA) - like structures (TLS) that were found to be enriched in the phloem stream and in mRNAs moving over chimeric graft junctions. Phenotypic and enzymatic assays on grafted plants indicated that mRNAs harboring a distinctive TLS can move from transgenic roots into wild-type leaves and from transgenic leaves into wild-type flowers or roots; these mRNAs can also be translated into proteins after transport. In addition, we provide evidence that di-cistronic mRNA:tRNA transcripts are frequently produced in *Arabidopsis thaliana* and are enriched in the population of graft-mobile mRNAs. Our results suggest that tRNA-derived sequences with predicted stem-bulge-stem-loop structures are sufficient to mediate mRNA transport and seem to be necessary for the mobility of a large number of endogenous transcripts that can move through graft junctions.

### **Imaging Reactive Oxygen Species-Induced Modifications in Living Systems**

*Giuseppe Maulucci, Goran Bačić, Lori Bridal, Harald HHW Schmidt, Bertrand Tavitian, Thomas Viel, Hideo Utsumi, A. Süha Yalçın, and Marco De Spirito*

Antioxidants & Redox Signaling, Vol. 24, No. 16, June 2016: 939-958.

[Abstract](#) | [Full Text HTML](#) | [Full Text PDF \(1424 KB\)](#) | [Full Text PDF with Links \(736 KB\)](#)

Lighting the way to protein-protein interactions: recommendations on best practices for bimolecular fluorescence complementation (BiFC) analyses

Ralph Bock and Joerg Kudla

Plant Cell 2016 tpc.16.00043; Advance Publication April 20, 2016; doi:10.1105/tpc.16.00043 **OPEN**  
<http://www.plantcell.org/content/early/2016/04/20/tpc.16.00043>

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Nitric oxide-fixation by non-symbiotic hemoglobin proteins in Arabidopsis thaliana under N-limited conditions.

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