Lit Lunch – October 4th, 2013

ELIZABETH

Science September 27, 2013

Sourcing Antibiotic Resistance

It is widely assumed that antibiotic resistance in farm animals contributes in a major way to antibiotic resistance in humans. **Mather *et al.*** (1514, published online 12 September; see the Perspective by **Woolhouse and Ward)** analyzed hundreds of genome sequences from *Salmonella* isolates collected from both livestock and patients in Scotland between 1990 and 2004. The relative contributions of animal-derived and human-derived sources of infection were quantified and the phylogenetic diversity of resistance profiles was matched with bacterial phylogenies. The results suggest that most human infections are caught from other humans rather than from livestock and that humans harbor a greater diversity of antibiotic resistance.

S-Nitrosylation: Specificity, Occupancy, and Interaction with Other Post-Translational Modifications

Alicia M. Evangelista, Mark J. Kohr, and Elizabeth Murphy

Antioxidants & Redox Signaling, Vol. 19, No. 11, October 2013: 1209-1219.

Specificity in S-Nitrosylation: A Short-Range Mechanism for NO Signaling?

Antonio Martínez-Ruiz, Inês M. Araújo, Alicia Izquierdo-Álvarez, Pablo Hernansanz-Agustín, Santiago Lamas, and Juan M. Serrador

Antioxidants & Redox Signaling, Vol. 19, No. 11, October 2013: 1220-1235.

Proteomic Approaches to Analyze Protein Tyrosine Nitration

Maria B. Feeney and Christian Schöneich

Antioxidants & Redox Signaling, Vol. 19, No. 11, October 2013: 1247-1256.

Genome-wide search for exonic variants affecting translational efficiency

- Quan Li, et al
  Nature Communications 4, Article number: 2260 Has great polysome profile.

Cas9 as a versatile tool for engineering biology pp957 - 963

Prashant Mali, Kevin M Esvelt and George M Church
doi:10.1038/nmeth.2649
This Perspective describes current and prospective advances in genome engineering made possible with the CRISPR-Cas9 system.

Nature Methods

The Plant Journal Content Alert (New Articles)

Synthetic nucleases for genome engineering in plants: prospects for a bright future
Holger Puchta*, Friedrich Fauser

By inducing double-strand breaks (DSB), it is possible to initiate DNA recombination. For a long time, it was not possible to use DSB induction for efficient genome engineering due to the lack of a way to target DSBs to specific sites. With the development of modified meganucleases and synthetic DNA binding domains, this limitation was overcome. Domains derived from zinc finger transcription factors or transcription activator-like effectors can be designed to recognise almost any DNA sequence. By fusing these domains to the endonuclease domains of a class II restriction enzyme, an active endonuclease dimer can be formed that introduces a site-specific DSB. Recent studies demonstrate that gene knock-outs via nonhomologous end joining or gene modification via homologous recombination are becoming routine in many plant species. By setting a single genomic DSB, the complete knock-out of a gene, the sequence-specific integration of foreign DNA, or the subtle modification of individual amino acids in a specific protein domain can be achieved. The induction of two or more DSBs allows for complex genomic rearrangements such as deletions, inversions, or the exchange of chromosome arms. The potential of controlled genome engineering in plants is tremendous. The recently discovered RNA-based CRISPR/Cas9 system as new tool to induce multiple DSBs or sophisticated technical applications, such as the *in planta* gene targeting system, are further steps in this development. At the moment, the focus still lies on the engineering of single genes; in the future, the engineering of whole genomes will become an option.

Plant, Cell & Environment Content Alert (New Articles)
Ammonium tolerance in the cyanobacterium *Synechocystis* sp. strain PCC 6803 and the role of the *psbA* multigene family
GUO-ZHENG DAI, BAO-SHENG QIU and KARL FORCHHAMMER
Accepted manuscript online: 24 SEP 2013 08:50PM EST | DOI: 10.1111/pce.12202

Archives of Biochemistry and Biophysics: Alert 23 September-29 September
The effects of nitroxyl (HNO) on H2O2 metabolism and possible mechanisms of HNO signaling
Original Research Article
Pages 120-129

Giffard RG, Macario AJ, de Macario EC.
The future of molecular chaperones and beyond.
J Clin Invest. 2013 Aug 1;123(8):3206-8.
PMID: 24063055 [PubMed - in process]

Pazos F, Pietrosemoli N, GarcÃa-MartÃn JA, Solano R.
Protein intrinsic disorder in plants.
Front Plant Sci. 2013 Sep 12;4:363. Review.
PMID: 24062761 [PubMed - as supplied by publisher]

Doyle SM, Genest O, Wickner S.
Protein rescue from aggregates by powerful molecular chaperone machines.
Nat Rev Mol Cell Biol. 2013 Oct;14(10):617-29.
PMID: 24061228 [PubMed - in process]

Zi J, Zhang J, Wang Q, Zhou B, Zhong J, Zhang C, Qiu X, Wen B, Zhang S, Fu X, Lin L, Liu S.
Stress Responsive Proteins Are Actively Regulated during Rice (Oryza sativa) Embryogenesis as Indicated by Quantitative Proteomics Analysis.
PLoS One. 2013 Sep 18;8(9):e74229.
PMID: 24058531 [PubMed - in process]

Anfelt J, HallstrÃ¶m B, Nielsen JB, UhlÃ©n M, Hudson EP.
Using transcriptomics to improve butanol tolerance in Synechocystis sp. PCC 6803.
Appl Environ Microbiol. 2013 Sep 20;. [Epub ahead of print]
PMID: 24056459 [PubMed - as supplied by publisher]

Noi K, Yamamoto D, Nishikori S, Arita-Morioka KI, Kato T, Ando T, Ogura T.
High-Speed Atomic Force Microscopic Observation of ATP-Dependent Rotation of the AAA+ Chaperone p97.
Structure. 2013 Sep 17;. [Epub ahead of print]
PMID: 24055316 [PubMed - as supplied by publisher]

Romero-Puertas MC, RodrÃguez-Serrano M, Sandalio LM.
Protein <i>S</i>-nitrosylation in plants under abiotic stress: an overview.
Front Plant Sci. 2013 Sep 20;4:373. Review.
PMID: 24065977 [PubMed - as supplied by publisher]

Silva L, Carvalho H.
Possible role of glutamine synthetase in the NO signaling response in root nodules by contributing to the antioxidant defenses.
Front Plant Sci. 2013 Sep 19;4:372.
PMID: 24065976 [PubMed]

Arc E, Galland M, Godin B, Cueff G, Rajjou L.
Nitric oxide implication in the control of seed dormancy and germination.
Front Plant Sci. 2013 Sep 19;4:346. Review.
PMID: 24065970 [PubMed - as supplied by publisher]

Guillas I, Puyaubert J, Baudouin E.
Nitric oxide-sphingolipid interplays in plant signalling: a new enigma from the Sphinx?
Front Plant Sci. 2013 Sep 12;4:341. Review.
PMID: 24062754 [PubMed - as supplied by publisher]

Schlicht M, Kombrink E.
The role of nitric oxide in the interaction of Arabidopsis thaliana with the biotrophic fungi, Golovinomyces orontii and Erysiphe pisi.
Front Plant Sci. 2013 Sep 9;4:351.
PMID: 24058365 [PubMed]

Spyrakis F, Lucas F, Bidon-Chanal A, Viappiani C, Guallar V, Luque FJ.
Comparative analysis of inner cavities and ligand migration in non-symbiotic AHb1 and AHb2.
Biochim Biophys Acta. 2013 Sep;1834(9):1957-67.
PMID: 23583621 [PubMed - indexed for MEDLINE]

Liu X, Jiang H, Gu Z, Roberts JW.
High-resolution view of bacteriophage lambda gene expression by ribosome profiling.
Proc Natl Acad Sci U S A. 2013 Jul 16;110(29):11928-33.
PMID: 23812753 [PubMed - indexed for MEDLINE]

Cell: Alert 23 September-29 September

Mitochondrial Cristae Shape Determines Respiratory Chain Supercomplexes Assembly and Respiratory Efficiency Original Research Article

Pages 160-171
Sara Cogliati, Christian Frezza, Maria Eugenia Soriano, Tatiana Varanita, Ruben Quintana-Cabrera, Mauro Corrado, Sara Cipolat, Veronica Costa, Alberto Casarin, Ligia C. Gomes, Ester Perales-Clemente, Leonardo Salviati, Patricio Fernandez-Silva, Jose A. Enriquez, Luca Scorrano

Molecular Cell: Alert 23 September-29 September

Proteasomes Activate Aggresome Disassembly and Clearance by Producing Unanchored Ubiquitin Chains Original Research Article

Pages 819-828
Rui Hao, Priyaanka Nanduri, Yanhua Rao, R. Scott Panichelli, Akihiro Ito, Minoru Yoshida, Tso-Pang Yao

FEBS Journal Content Alert (New Articles)

Thiol-Blocking Electrophiles Interfere with Labeling and Detection of Protein Sulfenic Acids
Julie A. Reisz, Erika Bechtold, S. Bruce King, Leslie B. Poole and Cristina M. Furdui
Accepted manuscript online: 18 SEP 2013 04:15AM EST | DOI: 10.1111/febs.12535

Fu X, Shi X, Yan L, Zhang H, Chang Z.
In vivo substrate diversity and preference of small heat shock protein IbpB as revealed by using a genetically incorporated photo-crosslinker.
J Biol Chem. 2013 Sep 17;. [Epub ahead of print]
PMID: 24045939 [PubMed - as supplied by publisher]

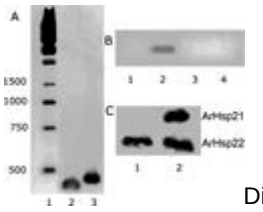
Peschek J, Braun N, Rohrberg J, Back KC, Kriehuber T, KastenmÃ¼ller A, Weinkauf S, Buchner J.
Regulated structural transitions unleash the chaperone activity of Î±B-crystallin.
Proc Natl Acad Sci U S A. 2013 Sep 16;. [Epub ahead of print]
PMID: 24043785 [PubMed - as supplied by publisher]

Vitlin Gruber A, Nisemblat S, Azem A, Weiss C.
The complexity of chloroplast chaperonins.
Trends Plant Sci. 2013 Sep 12;. [Epub ahead of print]
PMID: 24035661 [PubMed - as supplied by publisher]

Qin D, Fredrick K.
Analysis of polysomes from bacteria.
Methods Enzymol. 2013;530:159-72.
PMID: 24034320 [PubMed - in process]

FEBS Journal Content Alert: 280, 19 (October 2013)

Functional differentiation of small heat shock proteins in diapause-destined *Artemia* embryos (pages 4761–4772)
Allison M. King, Jantina Toxopeus and Thomas H. MacRae
Article first published online: 19 AUG 2013 | DOI: 10.1111/febs.12442



Diapause embryos of *Artemia franciscana* synthesize three distinct small heat shock proteins under transcriptional and translational regulation. As shown previously by RNAi, the small heat shock protein p26 influences embryo development and stress tolerance. In contrast, ArHsp21 has minimal impact on cyst stress tolerance. It was not possible to analyze ArHsp22 function because injection with dsRNA for ArHsp22 killed adults.

Cell: Alert 9 September-15 September

A Template for New Drugs against Alzheimer's Disease
Pages 1182-1184
Adriano Aguzzi, Aaron D. Gitler

Molecular Structure of β-Amyloid Fibrils in Alzheimer's Disease Brain Tissue Original Research Article
Pages 1257-1268
Jun-Xia Lu, Wei Qiang, Wai-Ming Yau, Charles D. Schwieters, Stephen C. Meredith, Robert Tycko

Molecular Cell: Alert 9 September-15 September

Proteasomes Activate Aggresome Disassembly and Clearance by Producing Unanchored Ubiquitin Chains Original Research Article
Available online 12 September 2013
Rui Hao, Priyaanka Nanduri, Yanhua Rao, R. Scott Panichelli, Akihiro Ito, Minoru Yoshida, Tso-Pang Yao

DAMIAN

Article 1:

AU - Stewart Lilley, Jodi L. Gan, Yinbo Graham, Ian A. Nemhauser, Jennifer L.
TI - The effects of DELLAs on growth change with developmental stage and brassinosteroid levels
JO - The Plant Journal
UR - http://dx.doi.org/10.1111/tpj.12280

Article 2:

A re-evaluation of the role of Arabidopsis NRT1.1 in high-affinity nitrate transport.
Anthony D.M. Glass and Zorica Kotur
Plant Physiol. pp.113.229161; First Published on October 2, 2013; doi:10.1104/pp.113.229161

KEITH

Prefoldin Plays a Role as a Clearance Factor in Preventing Proteasome Inhibitor-induced Protein Aggregation

The Journal of Biological Chemistry, 288, 27764-27776.

Akira Abe, Kazuko Takahashi-Niki, Yuka Takekoshi, Takashi Shimizu, Hirotake Kitaura[‡] Hiroshi Maita, Sanae M. M. Iguchi-Ariga and Hiroyoshi Ariga

Graduate School of Pharmaceutical Sciences, Hokkaido University, Kita-ku, Sapporo 060-0812 and Graduate School of Agriculture, Hokkaido University, Kita-ku, Sapporo 060-8589, Japan.

Prefoldin is a molecular chaperone composed of six subunits, PFD1–6, and prevents misfolding of newly synthesized nascent polypeptides. Although it is predicted that prefoldin, like other chaperones, modulates protein aggregation, the precise function of prefoldin against protein aggregation under physiological conditions has never been elucidated. In this study, we first established an anti-prefoldin monoclonal antibody that recognizes the prefoldin complex but not its subunits. Using this antibody, it was found that prefoldin was localized in the cytoplasm with dots in co-localization with polyubiquitinated proteins and that the number and strength of dots were increased in cells that had been treated with lactacystin, a proteasome inhibitor, and thapsigargin, an inducer of endoplasmic reticulum stress. Knockdown of prefoldin increased the level of SDS-insoluble ubiquitinated protein and reduced cell viability in lactacystin and thapsigargin-treated cells. Opposite results were obtained in prefoldin-overexpressed cells. It has been reported that mice harboring a missense mutation L110R of MM-1α/PFD5 exhibit neurodegeneration in the cerebellum. Although the prefoldin complex containing L110R MM-1α was properly formed in vitro and in cells derived from L110R MM-1α mice, the levels of ubiquitinated proteins and cytotoxicity were higher in L110R MM-1α cells than in wild-type cells under normal conditions and were increased by lactacystin and thapsigargin treatment, and growth of L110R MM-1α cells was attenuated. Furthermore, the polyubiquitinated protein aggregation level was increased in the brains of L110R MM-1α mice. These results suggest that prefoldin plays a role in quality control against protein aggregation and that dysfunction of prefoldin is one of the causes.

Reconstitution of the 26S proteasome reveals functional asymmetries in its AAA+ unfoldase

Nature Structural & Molecular Biology **20**, 1164–1172 (2013)

Robyn Beckwith, Eric Estrin, Evan J Worden & Andreas Martin

Department of Molecular and Cell Biology, University of California, Berkeley, Berkeley, California, USA.

The 26S proteasome is the major eukaryotic ATP-dependent protease, yet the detailed mechanisms used by the proteasomal heterohexameric AAA+ unfoldase to drive substrate degradation remain poorly understood. To perform systematic mutational analyses of individual ATPase subunits, we heterologously expressed the unfoldase subcomplex from *Saccharomyces cerevisiae* in *Escherichia coli* and reconstituted the proteasome *in vitro*. Our studies demonstrate that the six ATPases have distinct roles in degradation, corresponding to their positions in the spiral staircases adopted by the AAA+ domains in the absence or presence of substrate. ATP hydrolysis in subunits at the top of the staircases is critical for substrate engagement and translocation. Whereas the unfoldase relies on this vertical asymmetry for substrate processing, interaction with the peptidase exhibits three-fold symmetry with contributions from alternate subunits. These diverse functional asymmetries highlight how the 26S proteasome deviates from simpler, homomeric AAA+ proteases.

STEPHANIE

Stress granules and cell signaling: more than just a passing phase? – TIBS

- Nancy Kedersha,
- Pavel Ivanov,
- Paul Anderson

Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Smith 652, One Jimmy Fund Way, Boston, MA 02115, USA

Stress granules (SGs) contain translationally-stalled mRNAs, associated preinitiation factors, and specific RNA-binding proteins. In addition, many signaling proteins are recruited to SGs and/or influence their assembly, which is transient, lasting only until the cells adapt to stress or die. Beyond their role as mRNA triage centers, we posit that SGs constitute RNA-centric signaling hubs analogous to classical multiprotein signaling domains such as transmembrane receptor complexes. As signaling centers, SG formation communicates a ‘state of emergency’, and their transient existence alters multiple signaling pathways by intercepting and sequestering signaling components. SG assembly and downstream signaling functions may require a cytosolic phase transition facilitated by intrinsically disordered, aggregation-prone protein regions shared by RNA-binding and signaling proteins.

Hsp70 chaperone dynamics and molecular mechanism – TIBS

- Matthias P. Mayer

Zentrum für Molekulare Biologie der Universität Heidelberg (ZMBH), DKFZ-ZMBH-Alliance, Heidelberg, Germany

The chaperone functions of heat shock protein (Hsp)70 involve an allosteric control mechanism between the nucleotide-binding domain (NBD) and polypeptide substrate-binding domain (SBD): ATP binding and hydrolysis regulates the affinity for polypeptides, and polypeptide binding accelerates ATP hydrolysis. These data suggest that Hsp70s exist in at least two conformational states. Although structural

information on the conformation with high affinity for polypeptides has been available for several years, the conformation with an open polypeptide binding cleft was elucidated only recently. In addition, other biophysical studies have revealed a more dynamic picture of Hsp70s, shedding light on the molecular mechanism by which Hsp70s assist protein folding. In this review recent insights into the structure and mechanism of Hsp70s are discussed.

Students Propose Genetic Solutions to Societal Problems –Science

- Sue Wick, Mark Decker, David Matthes, and Robin Wright

Science 27 September 2013: 1467-1468. [DOI:10.1126/science.1230002]

IPlant - https://user.iplantcollaborative.org/dashboard/

FIONN

Spatial sequestration of misfolded proteins by a dynamic chaperone pathway enhances cellular fitness during stress

Stéphanie Escusa-Toret[1], Willianne I. M. Vonk[1] and Judith Frydman[1,2]

The extensive links between proteotoxic stress, protein aggregation and pathologies ranging from ageing to neurodegeneration underscore the importance of understanding how cells manage protein misfolding. Using live-cell imaging, we determine the fate of stress-induced misfolded proteins from their initial appearance until their elimination. Upon denaturation, misfolded proteins are sequestered from the bulk cytoplasm into dynamic endoplasmic reticulum (ER)-associated puncta that move and coalesce into larger structures in an energy-dependent but cytoskeleton-independent manner. These puncta, which we name Q-bodies, concentrate different misfolded and stress-denatured proteins en route to degradation, but do not contain amyloid aggregates, which localize instead to the insoluble protein deposit compartment. Q-body formation and clearance depends on an intact cortical ER and a complex chaperone network that is affected by rapamycin and impaired during chronological ageing. Importantly, Q-body formation enhances cellular _tness during stress. We conclude that spatial sequestration of misfolded proteins in Q-bodies is an early quality control strategy occurring synchronously with degradation to clear the cytoplasm of potentially toxic species.