August 10 – Lit Breakfast

Brehme M, Voisine C.
Model systems of protein-misfolding diseases reveal chaperone modifiers of proteotoxicity.
Dis Model Mech. 2016 Aug 1;9(8):823-838. PMID: 27491084 http://dmm.biologists.org/content/9/8/823

Kornprobst M, Turk M, Kellner N, Cheng J, Flemming D, KoÅ¡-Braun I, KoÅ¡ M, Thoms M, Berninghausen O, Beckmann R, Hurt E.
Architecture of the 90S Pre-ribosome: A Structural View on the Birth of the Eukaryotic Ribosome.
Cell. 2016 Jul 14;166(2):380-393. PMID: 27419870 [PubMed - as supplied by publisher]

Hoseini H, Pandey S, Jores T, Schmitt A, Franz-Wachtel M, Macek B, Buchner J, Dimmer KS, Rapaport D.
The cytosolic co-chaperone Sti1 is relevant for mitochondrial biogenesis and morphology.
FEBS J. 2016 Jul 14;. [Epub ahead of print] PMID: 27412066 [PubMed - as supplied by publisher]

Lindquist E, Solymosi K, Aronsson H.
Vesicles are persistent features of different plastids.
Traffic. 2016 Jul 12;. [Epub ahead of print] PMID: 27405297 [PubMed - as supplied by publisher]

Jiang D, Berger F.
Histone variants in plant transcriptional regulation.
Biochim Biophys Acta. 2016 Jul 10;. [Epub ahead of print] PMID: 27412913 [PubMed - as supplied by publisher]

Salmon L, Ahlstrom LS, Horowitz S, Dickson A, Brooks CL, Bardwell JC.
Capturing a dynamic chaperone-substrate interaction using NMR-informed molecular modeling.
J Am Chem Soc. 2016 Jul 14;. [Epub ahead of print] PMID: 27415450 [PubMed - as supplied by publisher]

Rousseau A, Bertolotti A.

An evolutionarily conserved pathway controls proteasome homeostasis.
Nature. 2016 Jul 27;. [Epub ahead of print] PMID: 27462806 [PubMed - as supplied by publisher]

Chen L, Chen Q, Kong L, Xia F, Yan H, Zhu Y, Mao P.
Proteomic and Physiological Analysis of the Response of Oat (Avena sativa) Seeds to Heat Stress under Different Moisture Conditions.
Front Plant Sci. 2016;7:896. PMID: 27446126 [PubMed]

Eichmann C, Tzitzilonis C, Nakamura T, Kwiatkowski W, Maslennikov I, Choe S, Lipton SA, Riek R.
S-Nitrosylation Induces Structural and Dynamical Changes in a Rhodanese Family Protein.
J Mol Biol. 2016 Jul 26;. [Epub ahead of print] PMID: 27473602 [PubMed - as supplied by publisher]

Hussain A, Mun BG, Imran QM, Lee SU, Adamu TA, Shahid M, Kim KM, Yun BW.
Nitric Oxide Mediated Transcriptome Profiling Reveals Activation of Multiple Regulatory Pathways in Arabidopsis thaliana.
Front Plant Sci. 2016;7:975. PMID: 27446194 [PubMed]

Schiffrin B, Calabrese AN, Devine PW, Harris SA, Ashcroft AE, Brockwell DJ, Radford SE.
Skp is a multivalent chaperone of outer-membrane proteins.
Nat Struct Mol Biol. 2016 Jul 25;. PMID: 27455461 [PubMed - as supplied by publisher]

Kim JH, Jung YJ, Choi B, Lee NL, Lee HJ, Kwak SY, Kwon Y, Na Y, Lee YS.
Overcoming HSP27-mediated resistance by altered dimerization of HSP27 using small molecules.
Oncotarget. 2016 Jul 16;. [Epub ahead of print] PMID: 27449291 [PubMed - as supplied by publisher]

Muthusamy SK, Dalal M, Chinnusamy V, Bansal KC.
Differential Regulation of Genes Coding for Organelle and Cytosolic ClpATPases under Biotic and Abiotic Stresses in Wheat.
Front Plant Sci. 2016;7:929. PMID: 27446158 [PubMed]

Knappe D, Goldbach T, Hatfield MP, Palermo NY, Weinert S, StrÃ¤ter N, Hoffmann R, Lovas S.
Proline-rich Antimicrobial Peptides Optimized for Binding to Escherichia coli Chaperone DnaK.
Protein Pept Lett. 2016 Jul 19;. PMID: 27449941 [PubMed - as supplied by publisher]

Kurganov BI.
Quantification of anti-aggregation activity of chaperones.
Int J Biol Macromol. 2016 Jul 22;. PMID: 27456122 [PubMed - as supplied by publisher]

Choudhary MK, Nomura Y, Shi H, Nakagami H, Somers DE.
Circadian Profiling of the Arabidopsis Proteome Using 2D-DIGE.
Front Plant Sci. 2016;7:1007.PMID: 27462335 [PubMed]

Kumar RR, Goswami S, Singh K, Dubey K, Singh S, Sharma R, Verma N, Kala YK, Rai GK, Grover M, Mishra DC, Singh B, Pathak H, Chinnusamy V, Rai A, Praveen S.
Identification of Putative RuBisCo Activase (TaRca1)-The Catalytic Chaperone Regulating Carbon Assimilatory Pathway in Wheat (Triticum aestivum) under the Heat Stress.
Front Plant Sci. 2016;7:986. PMID: 27462325 [PubMed]

Liu Y, Offler CE, Ruan YL.
Cell wall invertase promotes fruit set under heat stress by suppressing ROS-independent plant cell death.
Plant Physiol. 2016 Jul 26;. PMID: 27462084 [PubMed - as supplied by publisher]

Ding G, Chen P, Zhang H, Huang X, Zang Y, Li J, Li J, Wong J.
Regulation of Ubiquitin-like with PHD and RING Finger Domain 1 (UHRF1) Protein Stability by Heat Shock Protein 90 Chaperone Machinery.
J Biol Chem. 2016 Aug 3;. PMID: 27489107 [PubMed - as supplied by publisher]

Sung N, Lee J, Kim JH, Chang C, Tsai FT, Lee S.
2.4â€…Ã… resolution crystal structure of human TRAP1NM, the Hsp90 paralog in the mitochondrial matrix.
Acta Crystallogr D Struct Biol. 2016 Aug 1;72(Pt 8):904-11. PMID: 27487821 [PubMed - in process]

Chartron JW, Hunt KC, Frydman J.
Cotranslational signal-independent SRP preloading during membrane targeting.
Nature. 2016 Aug 3;. [PMID: 27487213 [PubMed - as supplied by publisher]

Schibich D, Gloge F, PÃ¶hner I, BjÃ¶rkholm P, Wade RC, von Heijne G, Bukau B, Kramer G.
Global profiling of SRP interaction with nascent polypeptides.
Nature. 2016 Aug 3;. [PMID: 27487212 [PubMed - as supplied by publisher]

Wickner RB.
Yeast and Fungal Prions.
Cold Spring Harb Perspect Biol. 2016 Aug 1;. [Epub ahead of print]
PMID: 27481532 [PubMed - as supplied by publisher]

Sousa R, Liao HS, CuÃ©llar J, Jin S, Valpuesta JM, Jin AJ, Lafer EM.
Clathrin-coat disassembly illuminates the mechanisms of Hsp70 force generation.
Nat Struct Mol Biol. 2016 Aug 1;. [Epub ahead of print]
PMID: 27478930 [PubMed - as supplied by publisher]

Marshall RS, McLoughlin F, Vierstra RD.
Autophagic Turnover of Inactive 26S Proteasomes in Yeast Is Directed by the Ubiquitin Receptor Cue5 and the Hsp42 Chaperone.
Cell Rep. 2016 Jul 27;. PMID: 27477278 [PubMed - as supplied by publisher]

Shah M, Su D, Scheliga JS, Pluskal T, Boronat S, Motamedchaboki K, Campos AR, Qi F, Hidalgo E, Yanagida M, Wolf DA.
A Transcript-Specific eIF3 Complex Mediates Global Translational Control of Energy Metabolism.
Cell Rep. 2016 Jul 27;. PMID: 27477275 [PubMed - as supplied by publisher]

Current Biology: Alert 3 August-9 August

Cytokinin and Auxin Display Distinct but Interconnected Distribution and Signaling Profiles to Stimulate Cambial Activity

Pages *1990-1997*

Juha Immanen, Kaisa Nieminen, Olli-Pekka Smolander, Mikiko Kojima, Juan Alonso Serra, Patrik Koskinen, Jing Zhang, Annakaisa Elo, Ari Pekka Mähönen, Nathaniel Street, Rishikesh P. Bhalerao, Lars Paulin, Petri Auvinen, Hitoshi Sakakibara, Ykä Helariutta

The Transcription Factor ATF5 Mediates a Mammalian Mitochondrial UPR

Pages *2037-2043*

Christopher J. Fiorese, Anna M. Schulz, Yi-Fan Lin, Nadine Rosin, Mark W. Pellegrino, Cole M. Haynes

Increasing Nitrogen Fixation and Seed Development in Soybean Requires Complex Adjustments of Nodule Nitrogen Metabolism and Partitioning Processes

Pages *2044-2051*

Amanda M Carter, Mechthild Tegeder

Lamin Mutations Accelerate Aging via Defective Export of Mitochondrial mRNAs through Nuclear Envelope Budding

Pages *2052-2059*

Yihang Li, Linda Hassinger, Travis Thomson, Baojin Ding, James Ashley, William Hassinger, Vivian Budnik

Arabidopsis NAP1 Regulates the Formation of Autophagosomes

Pages *2060-2069*

Pengwei Wang, Christine Richardson, Chris Hawes, Patrick J. Hussey

Analytical Biochemistry: Alert 31 July-6 August

Advanced negative detection method comparable to silver stain for SDS-PAGE separated proteins detection Original Research Article *Pages* *21-25*

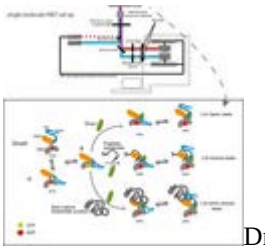
Xu Wang, Sun-Young Hwang, Wei-Tao Cong, Li-Tai Jin, Jung-Kap Choi

This actually looks pretty good from the pictures. I wonder if it is compatible with mass spec.

The FEBS Journal Content Alert: 283, 15 (August 2016)

Monitoring conformational heterogeneity of the lid of DnaK substrate-binding domain during its chaperone cycle (pages 2853–2868)

Rupa Banerjee, Gopal Gunanathan Jayaraj, Joshua Jebakumar Peter, Vignesh Kumar and Koyeli Mapa
Version of Record online: 4 JUL 2016 | DOI: 10.1111/febs.13769



DnaK or *E. coli* Hsp70 was subjected to single-molecule Förster resonance energy transfer (sm-FRET) measurements to capture distinct conformational states of the lid of its substrate-binding domain. We demonstrate that the lid of the chaperone adopts characteristics conformational states in the presence of nucleotides, J-domain cochaperone and different cellular substrates explaining finer details of DnaK chaperone function.

Molecular Cell: Alert 30 July-5 August

Methods for Optimizing CRISPR-Cas9 Genome Editing Specificity Review Article

Pages *355-370*

Josh Tycko, Vic E. Myer, Patrick D. Hsu

Structure of a Complete ATP Synthase Dimer Reveals the Molecular Basis of Inner Mitochondrial Membrane Morphology Original Research Article

Pages *445-456*

Alexander Hahn, Kristian Parey, Maike Bublitz, Deryck J. Mills, Volker Zickermann, Janet Vonck, Werner Kühlbrandt, Thomas Meier

Arabidopsis JINGUBANG is a Negative Regulator of Pollen Germination that Prevents Pollination in Moist Environments

Yan Ju, Liang Guo, Qiang Cai, Fei Ma, Qiao-Yun Zhu, Quan Zhang, and Sodmergen Sodmergen

Plant Cell 2016 tpc.16.00401; Advance Publication July 28, 2016; doi:10.1105/tpc.16.00401 **OPEN**

http://www.plantcell.org/content/early/2016/07/28/tpc.16.00401.abstract

Plant Journal – July 2016 – Special Issue on Synthetic Biology in Plants

http://EMBOJ.embopress.org/content/35/15/1597?etoc

Probing γ-secretase–substrate interactions at the single amino acid residue level Lucía Chávez-Gutiérrez and Bart De Strooper

Published online 01.07.2016

Photo-affinity cross-linking mapping of APP substrate interactions with different γ-secretase subunits suggests a succession of recruitment and

engagement steps leading up to intramembrane proteolysis.

http://EMBOJ.embopress.org/content/35/15/1603?etoc

Droplet organelles?

Edward M Courchaine, Alice Lu, and Karla M Neugebauer

Published online 29.06.2016

Non-membrane-bound cellular structures such as nucleoli, stress granules, Cajal and P bodies have been long established. Recent data reviewed by Neugebauer and colleagues delineate liquid–liquid phase separation processes that underlie the dynamic nature of these organelles composed of low-complexity proteins and RNA.

PLOS Genetics Volume 12(7) July 2016

Dynamics of Chloroplast Translation during Chloroplast Differentiation in Maize

Prakitchai Chotewutmontri, Alice Barkan

Perspective **Gene Regulation in Developing Chloroplasts Disentangled** William Zerges

Prefoldin Promotes Proteasomal Degradation of Cytosolic Proteins with Missense Mutations by Maintaining Substrate Solubility

Sophie A. Comyn, Barry P. Young, Christopher J. Loewen, Thibault Mayor

A High Temperature-Dependent Mitochondrial Lipase EXTRA GLUME1 Promotes Floral Phenotypic Robustness against Temperature Fluctuation in Rice (*Oryza sativa* L.)

Biyao Zhang, Shaohuan Wu, Yu'e Zhang, Ting Xu, Feifei Guo, Huashan Tang, Xiang Li, Pengfei Wang, Wenfeng Qian, Yongbiao Xue

The *Arabidopsis* KINβγ Subunit of the SnRK1 Complex Regulates Pollen Hydration on the Stigma by Mediating the Level of Reactive Oxygen Species in Pollen

Xin-Qi Gao, Chang Zhen Liu, Dan Dan Li, Ting Ting Zhao, Fei Li, Xiao Na Jia, Xin-Ying Zhao, Xian Sheng Zhang

PLOS Biology Volume 14(7) July 2016

The Mitochondrial Unfoldase-Peptidase Complex ClpXP Controls Bioenergetics Stress and Metastasis

Jae Ho Seo, Dayana B. Rivadeneira, M. Cecilia Caino, Young Chan Chae, David W. Speicher, Hsin-Yao Tang, Valentina Vaira, Silvano Bosari, Alessandro Palleschi, Paolo Rampini, Andrew V. Kossenkov, Lucia R. Languino, Dario C. Altieri

Exploitation of mitochondrial protein folding quality control via the mitochondrial unfoldase-peptidase complex ClpXP is critical for tumor cell proliferation, invasion, and metastatic competence, and represents a potential therapeutic target.

Cell: Alert 23 July-29 July

Compositional Control of Phase-Separated Cellular Bodies Original Research Article

Pages 651-663

Salman F. Banani, Allyson M. Rice, William B. Peeples, Yuan Lin, Saumya Jain, Roy Parker, Michael K. Rosen

Plant Cell

Examination of protein complexes gets SiMPull

Jennifer Mach

Plant Cell 2016 tpc.16.00590; Advance Publication July 27, 2016; doi:10.1105/tpc.16.00590 **OPEN**

http://www.plantcell.org/content/early/2016/07/27/tpc.16.00590

The FEBS Journal Content Alert: 283, 14 (July 2016)

Protease signaling in animal and plant-regulated cell death (pages 2577–2598)

Guy S. Salvesen, Anne Hempel and Nuria S. Coll

Version of Record online: 31 DEC 2015 | DOI: 10.1111/febs.13616

Regulated cell death mechanisms in animals and plants have at least one proteolytic component that plays a major role in controlling the pathway, and sometimes these proteases combine in networks to regulate cell death/survival decision nodes. Although similarities are found among animal and plant cell death proteases, the pathways that they govern are kingdom-specific with very little overlap.

Plant, Cell & Environment Content Alert (New Articles)

A new NO ledge in Chlamydomonas: when the old nitrate reductase (NR) meets amidoxime reducing component (ARC) to produce nitric oxide.

Hoai-Nam Truong and Christian Meyer

Accepted manuscript online: 20 JUL 2016 04:36AM EST | DOI: 10.1111/pce.12803

The FEBS Journal

The cytosolic co-chaperone Sti1 is relevant for mitochondrial biogenesis and morphology

Hoda Hoseini, Saroj Pandey, Tobias Jores, Anja Schmitt, Mirita Franz-Wachtel, Boris Macek, Johannes

Buchner, Kai Stefan Dimmer and Doron Rapaport
Accepted manuscript online: 14 JUL 2016 03:16AM EST | DOI: 10.1111/febs.13813

Glycerolipid synthesis and lipid trafficking in plant mitochondria
Morgane Michaud, William A. Prinz and Juliette Jouhet
Accepted manuscript online: 13 JUL 2016 06:05AM EST | DOI: 10.1111/febs.13812

The Plant Journal Content Alert: 86, 6 (June 2016)

P-class pentatricopeptide repeat protein PTSF1 is required for splicing of the plastid pre-tRNA^{Ile} in *Physcomitrella patens* (pages 493–503)
Seiya Goto, Yasuhiro Kawaguchi, Chieko Sugita, Mizuho Ichinose and Mamoru Sugita
Version of Record online: 20 JUN 2016 | DOI: 10.1111/tpj.13184
Significance Statement
Plastid gene expression is tightly regulated at the post-transcriptional level, often by pentatricopeptide repeat proteins. Loss of PPR proteins frequently leads to impaired organelle-related physiological and developmental functions, but the precise function of most PPR proteins are unknown. Here we characterized a P-class pentatricopeptide repeat protein in moss chloroplasts, which binds preferentially to domain III of the tRNA^{Ile} group II intron.

The Restorer-of-fertility-like 2 pentatricopeptide repeat protein and RNase P are required for the processing of mitochondrial orf291 RNA in Arabidopsis (pages 504–513)
Sota Fujii, Takamasa Suzuki, Philippe Giegé, Tetsuya Higashiyama, Nobuya Koizuka and Toshiharu Shikanai
Version of Record online: 15 JUL 2016 | DOI: 10.1111/tpj.13185
Significance Statement
Post-transcriptional modifications of mitochondrial RNA are often mediated by members of the nuclear-encoded pentatricopeptide repeat (PPR) protein superfamily, but little is known about how these proteins act because most PPR proteins lack enzymatic domains. Here we show that a PPR protein acts together with a RNase P to cleave a specific mitochondrial RNA.

Cell: Alert 9 July-15 July

Forces Driving Chaperone Action Original Research Article
Pages *369-379*
Philipp Koldewey, Frederick Stull, Scott Horowitz, Raoul Martin, James C.A. Bardwell

1,135 Genomes Reveal the Global Pattern of Polymorphism in *Arabidopsis thaliana* Original Research Article
Pages *481-491*
The 1001 Genomes Consortium

Indu

1: Shipman SL, Nivala J, Macklis JD, Church GM. Molecular recordings by directed CRISPR spacer acquisition. Science. 2016 Jul 29;353(6298):aaf1175. doi: 10.1126/science.aaf1175. Epub 2016 Jun 9. PubMed PMID: 27284167.

2: Briggs WR. PLANT SCIENCE. How do sunflowers follow the Sun--and to what end?
Science. 2016 Aug 5;353(6299):541-2. doi: 10.1126/science.aah4439. PubMed PMID:
27493168.

3: Abudayyeh OO, Gootenberg JS, Konermann S, Joung J, Slaymaker IM, Cox DB,
Shmakov S, Makarova KS, Semenova E, Minakhin L, Severinov K, Regev A, Lander ES,
Koonin EV, Zhang F. C2c2 is a single-component programmable RNA-guided RNA-targeting CRISPR effector. Science. 2016 Aug 5;353(6299):aaf5573. doi: 10.1126/science.aaf5573. Epub 2016 Jun 2. PubMed PMID: 27256883.

4: Mohanraju P, Makarova KS, Zetsche B, Zhang F, Koonin EV, van der Oost J. Diverse evolutionary roots and mechanistic variations of the CRISPR-Cas systems. Science. 2016 Aug 5;353(6299):aad5147. doi: 10.1126/science.aad5147. Review. PubMed PMID: 27493190.

5: Atamian HS, Creux NM, Brown EA, Garner AG, Blackman BK, Harmer SL. Circadian
regulation of sunflower heliotropism, floral orientation, and pollinator visits.
Science. 2016 Aug 5;353(6299):587-90. doi: 10.1126/science.aaf9793. PubMed PMID:
27493185.

6: Schrader J, Henneberg F, Mata RA, Tittmann K, Schneider TR, Stark H, Bourenkov
G, Chari A. The inhibition mechanism of human 20S proteasomes enables next-generation inhibitor design. Science. 2016 Aug 5;353(6299):594-8. doi: 10.1126/science.aaf8993. PubMed PMID: 27493187.

7: Qüesta JI, Song J, Geraldo N, An H, Dean C. Arabidopsis transcriptional repressor VAL1 triggers Polycomb silencing at FLC during vernalization. Science. 2016 Jul 29;353(6298):485-8. doi: 10.1126/science.aaf7354. PubMed PMID: 27471304.

Minsoo

1. Mol Cell. 2016 Aug 4;63(3):445-56. doi: 10.1016/j.molcel.2016.05.037. Epub 2016 Jun 30.

Structure of a Complete ATP Synthase Dimer Reveals the Molecular Basis of Inner Mitochondrial Membrane Morphology.

Hahn A(1), Parey K(1), Bublitz M(2), Mills DJ(1), Zickermann V(3), Vonck J(1), Kühlbrandt W(4), Meier T(5).

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(4)Department of Structural Biology, Max Planck Institute of Biophysics, Max-von-Laue-Str. 3, 60438 Frankfurt am Main, Germany. Electronic address: werner.kuehlbrandt@biophys.mpg.de. (5)Department of Structural Biology, Max Planck Institute of Biophysics, Max-von-Laue-Str. 3, 60438 Frankfurt am Main, Germany. Electronic address: t.meier@imperial.ac.uk.

We determined the structure of a complete, dimeric F1Fo-ATP synthase from yeast Yarrowia lipolytica mitochondria by a combination of cryo-EM and X-ray crystallography. The final structure resolves 58 of the 60 dimer subunits. Horizontal helices of subunit a in Fo wrap around the c-ring rotor, and a total of six vertical helices assigned to subunits a, b, f, i, and 8 span the membrane. Subunit 8 (A6L in human) is an evolutionary derivative of the bacterial b subunit. On the lumenal membrane surface, subunit f establishes direct contact between the two monomers. Comparison with a cryo-EM map of the F1Fo monomer identifies subunits e and g at the lateral dimer interface. They do not form dimer contacts but enable dimer formation by inducing a strong membrane curvature of ~100°. Our structure explains the structural basis of cristae formation in mitochondria, a landmark signature of eukaryotic cell morphology.
2. Mol Cell. 2016 Aug 4;63(3):355-70. doi: 10.1016/j.molcel.2016.07.004.

Methods for Optimizing CRISPR-Cas9 Genome Editing Specificity.

Tycko J(1), Myer VE(1), Hsu PD(2).

Author information:
(1)Editas Medicine, 300 Third Street, Cambridge, MA 02142, USA. (2)Editas Medicine, 300 Third Street, Cambridge, MA 02142, USA; Salk Institute for Biological Studies, 10010 North Torrey Pines Road, La Jolla, CA 92037, USA. Electronic address: patrick@salk.edu.

Advances in the development of delivery, repair, and specificity strategies for the CRISPR-Cas9 genome engineering toolbox are helping researchers understand gene function with unprecedented precision and sensitivity. CRISPR-Cas9 also

holds enormous therapeutic potential for the treatment of genetic disorders by directly correcting disease-causing mutations. Although the Cas9 protein has been shown to bind and cleave DNA at off-target sites, the field of Cas9 specificity is rapidly progressing, with marked improvements in guide RNA selection, protein and guide engineering, novel enzymes, and off-target detection methods. We review important challenges and breakthroughs in the field as a comprehensive practical guide to interested users of genome editing technologies, highlighting key tools and strategies for optimizing specificity. The genome editing community should now strive to standardize such methods for measuring and reporting off-target activity, while keeping in mind that the goal for specificity should be continued improvement and vigilance.

3. Nat Struct Mol Biol. 2016 Aug 1. doi: 10.1038/nsmb.3277. [Epub ahead of print]

Spiral architecture of the Hsp104 disaggregase reveals the basis for polypeptide translocation.

Yokom AL(1,)(2), Gates SN(1,)(2), Jackrel ME(3), Mack KL(3,)(4), Su M(1), Shorter J(3,)(4), Southworth DR(1).

Author information:
(1)Department of Biological Chemistry, Life Sciences Institute, University of Michigan, Ann Arbor, Michigan, USA. (2)Graduate Program in Chemical Biology, Life Sciences Institute, University of Michigan, Ann Arbor, Michigan, USA. (3)Department of Biochemistry and Biophysics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA. (4)Biochemistry and Molecular Biophysics Graduate Group, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA.

Hsp104, a conserved AAA+ protein disaggregase, promotes survival during cellular stress. Hsp104 remodels amyloids, thereby supporting prion propagation, and disassembles toxic oligomers associated with neurodegenerative diseases. However, a definitive structural mechanism for its disaggregase activity has remained

elusive. We determined the cryo-EM structure of wild-type Saccharomyces cerevisiae Hsp104 in the ATP state, revealing a near-helical hexamer architecture that coordinates the mechanical power of the 12 AAA+ domains for disaggregation. An unprecedented heteromeric AAA+ interaction defines an asymmetric seam in an apparent catalytic arrangement that aligns the domains in a two-turn spiral. N-terminal domains form a broad channel entrance for substrate engagement and Hsp70 interaction. Middle-domain helices bridge adjacent protomers across the nucleotide pocket, thus explaining roles in ATP hydrolysis and protein disaggregation. Remarkably, substrate-binding pore loops line the channel in a spiral arrangement optimized for substrate transfer across the AAA+ domains, thereby establishing a continuous path for polypeptide translocation.

Jesse

The LSM1-7 Complex Differentially Regulates Arabidopsis Tolerance to Abiotic Stress Conditions by Promoting Selective mRNA Decapping

Carlos Perea-Resa, Cristian Carrasco-López, Rafael Catalá,Veronika Turecková, Ondrej Novak, Weiping Zhang, Leslie Sieburth, José Manuel Jiménez-Gómez, and Julio Salinasa

The Plant Cell Feb 2016

http://www.plantcell.org/content/28/2/505.full.pdf+html?sid=e4656bc6-f236-4d33-a891-1e27cfff9f8f

In eukaryotes, the decapping machinery is highly conserved and plays an essential role in controlling mRNA stability, a key step in the regulation of gene expression. Yet, the role of mRNA decapping in shaping gene expression profiles in response t o environmental cues and the operating molecular mechanisms are poorly underst ood. Here, we provide genetic and molecular evidence that a component of the dec apping machinery, the LSM1-7 complex, plays a critical role in plant tolerance to ab

iotic stresses. Our results demonstrate that, depending on the stress, the complex f rom Arabidopsis thaliana interacts with different selected stress-inducible transcript s targeting them for decapping and subsequent degradation. This interaction ensur es the correct turnover of the target transcripts and, consequently, the appropriate patterns of downstream stressresponsive gene expression that are required for pla nt adaptation. Remarkably, among the selected target transcripts of the LSM1-7 co mplex are those encoding NCED3 and NCED5, two key enzymes in abscisic acid (ABA) biosynthesis. We demonstrate that the complex modulates ABA levels in Ara bidopsis exposed to cold and high salt by differentially controlling NCED3 and NCE D5 mRNA turnover, which represents a new layer of regulation in ABA biosynthesi s in response to abiotic stress. Our findings uncover an unanticipated functional pla sticity of the mRNA decapping machinery to modulate the relationship between pla nts and their environment.

Keith

Structural basis for the antifolding activity of a molecular chaperone.

Nature. 2016 Aug 8. doi: 10.1038/nature18965. [Epub ahead of print]

Huang C1, Rossi P1, Saio T1, Kalodimos CG1.

1Department of Biochemistry, Molecular Biology &Biophysics, University of Minnesota, Minneapolis, Minnesota 55455, USA.

Molecular chaperones act on non-native proteins in the cell to prevent their aggregation, premature folding or misfolding. Different chaperones often exert distinct effects, such as acceleration or delay of folding, on client proteins via mechanisms that are poorly understood. Here we report the solution structure of SecB, a chaperone that exhibits strong antifolding activity, in complex with alkaline phosphatase and maltose-binding protein captured in their unfolded states. SecB

uses long hydrophobic grooves that run around its disk-like shape to recognize and bind to multiple hydrophobic segments across the length of non-native proteins. The multivalent binding mode results in proteins wrapping around SecB. This unique complex architecture alters the kinetics of protein binding to SecB and confers strong antifolding activity on the chaperone. The data show how the different architectures of chaperones result in distinct binding modes with non-native proteins that ultimately define the activity of the chaperone.

Stabilizing the Hsp70-Tau Complex Promotes Turnover in Models of Tauopathy.

Cell Chem Biol. 2016 Aug 3. pii: S2451-9456(16)30217-3. doi: 10.1016/j.chembiol.2016.04.014. [Epub ahead of print]

Young ZT1, Rauch JN1, Assimon VA1, Jinwal UK2, Ahn M3, Li X1, Dunyak BM1, Ahmad A3, Carlson GA4, Srinivasan SR1, Zuiderweg ER5, Dickey CA2, Gestwicki JE6.

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4McLaughlin Research Institute, Great Falls, MT 59405, USA.
5Department of Biological Chemistry, University of Michigan, Ann Arbor, MI 48109, USA.
6Department of Pharmaceutical Chemistry, University of California at San Francisco, San Francisco, CA 94158, USA; Sandler Neuroscience Center, University of California at San Francisco, Room 311, 675 Nelson Rising Lane, San Francisco, CA 94158, USA.

Heat shock protein 70 (Hsp70) is a chaperone that normally scans the proteome and initiates the turnover of some proteins (termed clients) by linking them to the

degradation pathways. This activity is critical to normal protein homeostasis, yet it appears to fail in diseases associated with abnormal protein accumulation. It is not clear why Hsp70 promotes client degradation under some conditions, while sparing that protein under others. Here, we used a combination of chemical biology and genetic strategies to systematically perturb the affinity of Hsp70 for the model client, tau. This approach revealed that tight complexes between Hsp70 and tau were associated with enhanced turnover while transient interactions favored tau retention. These results suggest that client affinity is one important parameter governing Hsp70-mediated quality control.

The Molecular Chaperone Hsp70 Promotes the Proteolytic Removal of Oxidatively Damaged Proteins by the Proteasome.

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One hallmark of aging is the accumulation of protein aggregates, promoted by the unfolding of oxidized proteins. Unraveling the mechanism by which oxidized proteins are degraded may provide a basis to delay the early onset of features, such as protein aggregate formation, that contribute to the aging phenotype. In

order to prevent aggregation of oxidized proteins, cells recur to the 20S proteasome, an efficient turnover proteolysis complex. It has previously been shown that upon oxidative stress the 26S proteasome, another form, dissociates into the 20S form. A critical player implicated in its dissociation is the Heat Shock Protein 70 (Hsp70), which promotes an increase in free 20S proteasome and, therefore, an increased capability to degrade oxidized proteins. The aim of this study was to test whether or not Hsp70 is involved in cooperating with the 20S proteasome for a selective degradation of oxidatively damaged proteins. Our results demonstrate that Hsp70 expression is induced in HT22 cells as a result of mild oxidative stress conditions. Furthermore, Hsp70 prevents the accumulation of oxidized proteins and directly promotes their degradation by the 20S proteasome. In contrast the expression of the Heat shock cognate protein 70 (Hsc70) was not changed in recovery after oxidative stress and Hsc70 has no influence on the removal of oxidatively damaged proteins. We were able to demonstrate in HT22 cells, in brain homogenates from 129/SV mice and in vitro, that there is an increased interaction of Hsp70 with oxidized proteins, but also with the 20S proteasome, indicating a role of Hsp70 in mediating the interaction of oxidized proteins with the 20S proteasome. Thus, our data clearly implicate an involvement of Hsp70 oxidatively damaged protein degradation by the 20S proteasome.

Hsp90 directly interacts, in vitro, with amyloid structures and modulates their assembly and disassembly.

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BACKGROUND:
The 90kDa heat shock protein (Hsp90) participates in regulating the homeostasis of cellular proteins and was considered one of the key chaperones involved in the control and regulation of amyloid deposits. Hsp90 interacts with the amyloid protein tau through tau aggregation-prone regions, including the VQIVYK hexapeptide motif. This hexapeptide, which self-aggregates, forming amyloid fibrils, is widely used to model amyloid formation mechanisms. Despite evidence showing that Hsp90 interacts directly with Ac-VQIVYK-NH2, its role in the hexapeptide fibrillation process and its binding to peptide structures have not yet been determined.
METHODS:
Various biochemical and biophysical techniques, including ultracentrifugation, spectrophotometry, spectrofluorimetry, and electron microscopy, were employed to assess the effects of Hsp90 on Ac-VQIVYK-NH2 assembly and disassembly processes.
RESULTS:
At sub-stoichiometric concentrations, Hsp90 bound directly to Ac-VQIVYK-NH2 amyloid structures in vitro, with each Hsp90 dimer interacting with an amyloid structure made of around 50 hexapeptide subunits. Hsp90 inhibited Ac-VQIVYK-NH2 assembly by increasing the critical concentrations of Ac-VQIVYK-NH2 required for assembly. Hsp90 also inhibited the disassembly of Ac-VQIVYK-NH2 amyloid fibrils and promoted their rescue.
CONCLUSIONS:
A model explaining the dual effect of Hsp90 on the Ac-VQIVYK-NH2 amyloid fibrillation process has been proposed.
GENERAL SIGNIFICANCE:
These in vitro results provide new insights into the possible roles of molecular chaperones in modulating amyloid structures by limiting the spread of toxic species.