Indu

1. **Mitochondrial endonuclease G mediates breakdown of paternal mitochondria upon fertilization.**
Zhou Q, Li H, Li H, Nakagawa A, Lin JL, Lee ES, Harry BL, Skeen-Gaar RR, Suehiro Y, William D, Mitani S, Yuan HS, Kang BH, Xue D.
Science. 2016 Jun 23. pii: aaf4777. [Epub ahead of print]
PMID: 27338704 [PubMed - as supplied by publisher]
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2. **ER-mitochondria contacts couple mtDNA synthesis with mitochondrial division in human cells.**
Lewis SC, Uchiyama LF, Nunnari J.
Science. 2016 Jul 15;353(6296):aaf5549. doi: 10.1126/science.aaf5549.
PMID: 27418514 [PubMed - in process]
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Minsoo

1. Mol Cell. 2016 Jul 21;63(2):229-39. doi: 10.1016/j.molcel.2016.06.016.

A Small Molecule That Protects the Integrity of the Electron Transfer Chain Blocks the Mitochondrial Apoptotic Pathway.

Jiang X(1), Li L(2), Ying Z(1), Pan C(1), Huang S(1), Li L(1), Dai M(1), Yan B(1), Li M(1), Jiang H(1), Chen S(1), Zhang Z(1), Wang X(3).

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In response to apoptotic stimuli, mitochondria in mammalian cells release cytochrome c and other apoptogenic proteins, leading to the subsequent activation of caspases and apoptotic cell death. This process is promoted by the pro-apoptotic members of the Bcl-2 family of proteins, such as Bim and Bax, which, respectively, initiate and execute cytochrome c release from the mitochondria. Here we report the discovery of a small molecule that efficiently blocks Bim-induced apoptosis after Bax is activated on the mitochondria. The cellular target of this small molecule was identified to be the succinate dehydrogenase subunit B (SDHB) protein of complex II of the mitochondrial electron transfer chain (ETC). The molecule protects the integrity of the ETC and

allows treated cells to continue to proliferate after apoptosis induction. Moreover, this molecule blocked dopaminergic neuron death and reversed Parkinson-like behavior in a rat model of Parkinson's disease.

2. Mol Cell. 2016 Jul 21;63(2):240-8. doi: 10.1016/j.molcel.2016.05.040. Epub 2016 Jul 7.

Redox Nanodomains Are Induced by and Control Calcium Signaling at the ER-Mitochondrial Interface.

Booth DM(1), Enyedi B(2), Geiszt M(2), Várnai P(2), Hajnóczky G(3).

Author information:
(1)MitoCare Center, Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA 19107, USA. (2)Department of Physiology, Faculty of Medicine, Semmelweis University, 1444 Budapest, Hungary. (3)MitoCare Center, Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA 19107, USA. Electronic address: gyorgy.hajnoczky@jefferson.edu.

The ER-mitochondrial interface is central to calcium signaling, organellar dynamics, and lipid biosynthesis. The ER and mitochondrial membranes also host sources and targets of reactive oxygen species (ROS), but their local dynamics and relevance remained elusive since measurement and perturbation of ROS at the organellar interface has proven difficult. Employing drug-inducible synthetic ER-mitochondrial linkers, we overcame this problem and demonstrate that the ER-mitochondrial interface hosts a nanodomain of H2O2, which is induced by cytoplasmic [Ca(2+)] spikes and exerts a positive feedback on calcium oscillations. H2O2 nanodomains originate from the mitochondrial cristae, which are compressed upon calcium signal propagation to the mitochondria, likely due to Ca(2+)-induced K(+) and concomitant water influx to the matrix. Thus, ER-mitochondrial H2O2 nanodomains represent a component of inter-organelle communication, regulating calcium signaling and mitochondrial activities.

3. Plant J. 2016 Jul 18. doi: 10.1111/tpj.13276. [Epub ahead of print]

Retrograde signalling caused by heritable mitochondrial dysfunction is partially mediated by ANAC017 and improves plant performance.

Van Aken O(1), Ford E(1), Lister R(1), Huang S(1), Millar AH(1).

Author information:
(1)ARC Centre of Excellence in Plant Energy Biology, Faculty of Science, Bayliss Building M316, The University of Western Australia, 35 Stirling Highway, Crawley, 6009, Western Australia, Australia.

Mitochondria are crucial for plant viability and are able to communicate information on their functional status to the cellular nucleus via retrograde signalling, thereby affecting gene expression. It is currently unclear if retrograde signalling in response to constitutive mitochondrial biogenesis defects is mediated by the same pathways as those triggered during acute mitochondrial dysfunction. Furthermore, it is unknown if retrograde signalling can effectively improve plant performance when mitochondrial function is constitutively impaired. Here we show that retrograde signalling in mutants defective in mitochondrial proteins RNA polymerase rpotmp or prohibitin atphb3 can be suppressed by knocking out the transcription factor ANAC017. Genome-wide RNA-seq expression analysis revealed that ANAC017 is almost solely responsible for the most dramatic transcriptional changes common to rpotmp and atphb3 mutants, regulating classical marker genes such as alternative oxidase 1a (AOX1a) and also previously-uncharacterised DUF295 genes that appear to be new retrograde markers. In contrast, ANAC017 does not regulate intra-mitochondrial gene expression or transcriptional changes unique to either rpotmp or atphb3 genotype, suggesting the existence of currently unknown signalling cascades. The data show that ANAC017 function extends beyond common retrograde transcriptional responses and affects downstream protein abundance and enzyme activity of alternative oxidase, as well as steady state energy metabolism in atphb3 plants. Furthermore, detailed growth analysis revealed that ANAC017-dependent retrograde signalling provides benefits for growth and productivity in plants with mitochondrial defects. In conclusion, ANAC017 plays a key role in both biogenic and operational mitochondrial retrograde signalling, and improves plant performance when mitochondrial function is constitutively impaired.

Alyssa

A simple, flexible and high-throughput cloning system for plant genome editing via CRISPR-Cas system

Hyeran Kim, Sang-Tae Kim, Jahee Ryu, Min Kyung Choi, Jiyeon Kweon, Beum-Chang Kang, Hyo-Min Ahn, Suji Bae, Jungeun Kim, Jin-Soo Kim, and Sang-Gyu Kim

Abstract
CRISPR-Cas9 system is now widely used to edit a target genome in animals and plants. Cas9 protein derived from *Streptococcus pyogenes* (SpCas9) cleaves double-stranded DNA targeted by a chimeric single-guide RNA (sgRNA). For plant genome editing, *Agrobacterium*-mediated T-DNA transformation has been broadly used to express Cas9 proteins and sgRNAs under the control of CaMV 35S and U6/U3 promoter, respectively. We here developed a simple and high-throughput binary vector system to clone a 19−20 bp of sgRNA, which binds to the reverse complement of a target locus, in a large T-DNA binary vector containing an SpCas9 expressing cassette. Two-step cloning procedures: (1) annealing two target-specific oligonucleotides with overhangs specific to the *Aar*I restriction enzyme site of the binary vector; and (2) ligating the annealed oligonucleotides into the two *Aar*I sites of the vector, facilitate the

high-throughput production of the positive clones. In addition, Cas9-coding sequence and U6/U3 promoter can be easily exchanged via the Gateway™ system and unique *Eco*RI/*Xho*I sites on the vector, respectively. We examined the mutation ratio and patterns when we transformed these constructs into *Arabidopsis thaliana* and a wild tobacco, *Nicotiana attenuata*. Our vector system will be useful to generate targeted large-scale knock-out lines of model as well as non-model plant.

Ian

RNA-seq Analysis of δ9-Tetrahydrocannabinol-treated T Cells Reveals Altered Gene Expression Profiles That Regulate Immune Response and Cell Proliferation*

Xiaoming Yang, Marpe Bam, Prakash S. Nagarkatti and Mitzi Nagarkatti[1]

Abstract

Marijuana has drawn significant public attention and concern both for its medicinal and recreational use. Δ9-Tetrahydrocannabinol (THC), which is the main bioactive component in marijuana, has also been shown to possess potent anti-inflammatory properties by virtue of its ability to activate cannabinoid receptor-2 (CB-2) expressed on immune cells. In this study, we used RNA-seq to quantify the transcriptomes and transcript variants that are differentially regulated by THC in super antigen-activated lymph node cells and $CD4^+$ T cells. We found that the expressions of many transcripts were altered by THC in both total lymph node cells and $CD4^+$ T cells. Furthermore, the abundance of many miRNA precursors and long non-coding RNAs was dramatically altered in THC-treated mice. For example, the expression of miR-17/92 cluster and miR-374b/421 cluster was down-regulated by THC. On the other hand miR-146a, which has been shown to induce apoptosis, was up-regulated by THC. Long non-coding RNAs that are expressed from the opposite strand of *CD27* and *Appbp2* were induced by THC. In addition, THC treatment also caused alternative promoter usage and splicing. The functions of those altered transcripts were mainly related to immune response and cell proliferation.

Jesse

Identification and Characterization of Maize salmon silks Genes Involved in Insecticidal Maysin Biosynthesis

María Isabel Casas, María Lorena Falcone-Ferreyra, Nan Jiang,b María Katherine Mejía-Guerra, Eduardo Rodríguez,Tyler Wilson, Jacob Engelmeier, Paula Casati, and Erich Grotewoldb

The century-old maize (Zea mays) salmon silks mutation has been linked to the absence of maysin. Maysin is a C-glycosyl flavone that, when present in silks, confers natural resistance to the maize earworm (Helicoverpa zea), which is one of the most damaging pests of maize in America. Previous genetic analyses predicted Pericarp Color1 (P1; R2R3-MYB transcription factor) to be epistatic to the sm mutation. Subsequent studies identified two loci as being capable of conferring salmon silks phenotypes, salmon silks1 (sm1) and sm2. Benefitting from available sm1 and sm2

mapping information and from knowledge of the genes regulated by P1, we describe here the molecular identification of the Sm1 and Sm2 gene products. Sm2 encodes a rhamnosyl transferase (UGT91L1) that uses isoorientin and UDP-rhamnose as substrates and converts them to rhamnosylisoorientin. Sm1 encodes a multidomain UDP-rhamnose synthase (RHS1) that converts UDP-glucose into UDP-Lrhamnose. Here, we demonstrate that RHS1 shows unexpected substrate plasticity in converting the glucose moiety in rhamnosylisoorientin to 4-keto-6-deoxy glucose, resulting in maysin. Both Sm1 and Sm2 are direct targets of P1, as demonstrated by chromatin immunoprecipitation experiments. The molecular characterization of Sm1 and Sm2 described here completes the maysin biosynthetic pathway, providing powerful tools for engineering tolerance to maize earworm in maize and other plants.

The Plant Cell, Vol. 28: 1297–1309, June 2016

The Proteasome Stress Regulon Is Controlled by a Pair of NAC Transcription Factors in Arabidopsis
Nicholas P. Gladman, Richard S. Marshall, Kwang-Hee Lee, and Richard D. Vierstra

Proteotoxic stress, which is generated by the accumulation of unfolded or aberrant proteins due to environmental or cellular perturbations, can be mitigated by several mechanisms, including activation of the unfolded protein response and coordinated increases in protein chaperones and activities that direct proteolysis, such as the 26S proteasome. Using RNA-seq analyses combined with chemical inhibitors or mutants that induce proteotoxic stress by impairing 26S proteasome capacity, we defined the transcriptional network that responds to this stress in Arabidopsis thaliana. This network includes genes encoding core and assembly factors needed to build the complete 26S particle, alternative proteasome capping factors, enzymes involved in protein ubiquitylation/deubiquitylation and cellular detoxification, protein chaperones, autophagy components, and various transcriptional regulators. Many loci in this proteasome-stress regulon contain a consensus cis-element upstream of the transcription start site, which was previously identified as a binding site for the NAM/ATAF1/CUC2 78 (NAC78) transcription factor. Double mutants disrupting NAC78 and its closest relative NAC53 are compromised in the activation of this regulon and notably are strongly hypersensitive to the proteasome inhibitors MG132 and bortezomib. Given that NAC53 and NAC78 homo- and heterodimerize, we propose that they work as a pair in activating the expression of numerous factors that help plants survive proteotoxic stress and thus play a central regulatory role in maintaining protein homeostasis.

The Plant Cell, Vol. 28: 1279–1296, June 2016

Keith

Use of evolutionary information in the fitting of atomic level protein models in low resolution cryo-EM map of a protein assembly improves the accuracy of the fitting.

Joseph AP1, Swapna LS2, Rakesh R3, Srinivasan N4

J Struct Biol. 2016 Jul 18.

1National Centre for Biological Sciences, TIFR, UAS-GKVK Campus, Bellary road, Bangalore 560065. India; Institute of Structural and **Molecular** Biology, Department of Biological Sciences, Birkbeck College, University of London, Malet street, London WC1E 7HX, UK.
2**Molecular** Biophysics Unit, Indian Institute of Science, Bangalore 560012, India; **Molecular** Structure and Function program, Hospital for Sick Children, Toronto, Canada.
3**Molecular** Biophysics Unit, Indian Institute of Science, Bangalore 560012, India.
4**Molecular** Biophysics Unit, Indian Institute of Science, Bangalore 560012, India.

Protein-protein interface residues, especially those at the core of the interface, exhibit higher conservation than residues in solvent exposed regions. Here, we explore the ability of this differential conservation to evaluate fittings of atomic models in low-resolution cryo-EM maps and select models from the ensemble of solutions that are often proposed by different model fitting techniques. As a prelude, using a non-redundant and high-resolution structural dataset involving 125 permanent and 95 transient complexes, we confirm that core interface residues are conserved significantly better than nearby non-interface residues and this result is used in the cryo-EM map analysis. From the analysis of inter-component interfaces in a set of fitted models associated with low-resolution cryo-EM maps of ribosomes, **chaperones** and proteasomes we note that a few poorly conserved residues occur at interfaces. Interestingly a few conserved residues are not in the interface, though they are close to the interface. These observations raise the potential requirement of refitting the models in the cryo-EM maps. We show that sampling an ensemble of models and selection of models with high residue conservation at the interface and in good agreement with the density helps in improving the accuracy of the fit. This study indicates that evolutionary information can serve as an additional input to improve and validate fitting of atomic models in cryo-EM density maps.

dFOXO Activates Large and Small Heat Shock Protein Genes in Response to Oxidative Stress to Maintain Proteostasis in Drosophila.

J Biol Chem. 2016 Jul 19.

Brandeis University, United States.

Donovan MR1, Marr MT 2nd2.

Maintaining protein homeostasis is critical for survival at the cellular and organismal level. Cells express a family of **molecular chaperones**, the heat shock proteins, during times of oxidative stress to protect against proteotoxicity. We have identified a second stress responsive transcription factor, dFOXO, that works alongside the heat shock

transcription factor (HSF) to activate transcription of both the small heat shock protein and the large heat shock protein genes. This expression likely protects cells from protein misfolding associated with oxidative stress. Here we identify the regions of the Hsp70 promoter essential for FOXO-dependent transcription using in vitro methods and find a physiological role for FOXO-dependent expression of heatshock proteins in vivo.

Enhanced salt tolerance in tomato plants constitutively expressing heat-shock protein in the endoplasmic reticulum

Genet Mol Res. 2016 Jul 14;15(2).

Fu C1, Liu XX1, Yang WW1, Zhao CM1, Liu J1.

1Shandong Provincial Key Laboratory of Plant Stress Research, College of Life Science, Shandong Normal University, Jinan, Shandong, China.

The accumulation of unfolded or misfolded proteins in the endoplasmic reticulum (ER) causes ER stress and activates the unfolded protein response (UPR) signaling pathway. The UPR signaling pathway is associated with plant responses to adverse environmental conditions. Thus, changes in the UPR signaling pathway might affect plant abiotic tolerance. Here, the role of ER small heat-shock protein (ER-sHSP) in improving plant resistance to salt stress was explored. Under salt stress conditions, ER-sHSP transgenic plants were found to have more vigorous roots, maintain a higher relative water content, absorb less Na(+), accumulate more osmolytes and Ca(2+), and sustain less damage to the photosystem, compared to wild-type non-transgenic plants. Furthermore, we found that the constitutive expression of ER-sHSP under salt stress depressed the expression of other ER **molecular chaperones**. These results indicate that the constitutive expression of ER-sHSP enhanced salinity tolerance of tomato plants significantly, and alleviated the ER stress caused by the salt stress in plant cells.

Heat shock protein 90 kDa Hsp90 has a second functional interaction site with the mitochondrial import receptor Tom70.

J Biol Chem. 2016 Jul 8.

Zanphorlin LM1, Lima TB1, Wong MJ2, Balbuena TS3, Minetti CA4, Remeta DP4, Young JC2, Barbosa LR5, Gozzo FC1, Ramos CH6.

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To accomplish its crucial role, mitochondria require proteins that are produced in the cytosol, delivered by cytosolic Hsp90 and translocated to its interior by the Translocase Outer Membrane/TOM complex. Hsp90 is a dimeric **molecular** chaperone and its function is modulated by its interaction with a large variety of co-**chaperones** expressed within the cell. An important family of co-**chaperones** is characterized by the presence of one TPR (tetratricopeptide repeat) domains which bind to the C-terminal MEEVD motif of Hsp90. These include Tom70, an important component of the TOM complex. Despite a wealth of studies conducted on the relevance of Tom70/Hsp90 complex formation, there is a dearth of information regarding the exact **molecular** mode of interaction. To help fill this void, we have employed a combined experimental strategy consisting of crosslinking/mass spectrometry to investigate binding of the C-terminal Hsp90 domain to the cytosolic domain of Tom70. This approach has identified a novel region of contact between C-Hsp90 and Tom70, a finding that is confirmed by probing the corresponding peptides derived from crosslinking experiments via isothermal titration calorimetry and mitochondrial import assays. The data generated in this study are combined to input constraints for a **molecular** model of the Hsp90/Tom70 interaction, which has been validated by small angle X-ray scattering, hydrogen/deuterium exchange, and mass spectrometry. The resultant model suggests that only one of the MEEVD motifs within dimeric Hsp90 contacts Tom70. Collectively, our findings provide significant insight on the mechanisms by which preproteins interact with Hsp90 and are translocated via Tom70 to the mitochondria.

Probing Allosteric Inhibition Mechanisms of the Hsp70 Chaperone Proteins Using Molecular Dynamics Simulations and Analysis of the Residue Interaction Networks.

J Chem Inf Model. 2016 Jul 22. [Epub ahead of print]

Stetz G, Verkhivker GM.

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2Chapman University School of Pharmacy, Irvine, CA 92618, USA

Although molecular mechanisms of allosteric regulation in the Hsp70 chaperones have been extensively studied at both structural and functional levels, the current understanding of allosteric inhibition of chaperone activities by small molecules is still lacking. In the current study, using a battery of computational approaches we probed allosteric inhibition mechanisms of E. coli Hsp70 (DnaK) and human Hsp70 proteins by small molecule inhibitors PET-16 and novolactone. Molecular dynamics simulations and binding free energy analysis were combined with network-based modeling of residue interactions and allosteric communications to systematically characterize and compare molecular signatures of the apo form, substrate-bound, and inhibitor-bound chaperone complexes. The results suggested a mechanism by which the allosteric inhibitors may

leverage binding energy hotspots in the interaction networks to stabilize a specific conformational state and impair the inter-domain allosteric control. Using the network-based centrality analysis and community detection, we demonstrated that substrate binding may strengthen the connectivity of local interaction communities, leading to a dense interaction network that can promote an efficient allosteric communication. In contrast, binding of PET-16 to DnaK may induce significant dynamic changes and lead to a fractured interaction network and impaired allosteric communications in the DnaK complex. By using a mechanistic-based analysis of distance fluctuation maps and allosteric propensities of protein residues, we determined that the allosteric network in the PET-16 complex may be small and localized due to the reduced communication and low cooperativity of the substrate binding loops, which may promote the higher rates of substrate dissociation and the decreased substrate affinity. In comparison with the significant effect of PET-16, binding of novolactone to HSPA1A may cause only moderate network changes and preserve allosteric coupling between the allosteric pocket and the substrate binding region. The impact of novolactone on the conformational dynamics and allosteric communications in the HSPA1A complex was comparable to the substrate effect, which is consistent with the experimental evidence that PET-16, but not novolactone binding, can significantly decrease substrate affinity. We argue that the unique dynamic and network signatures of PET-16 and novolactone may be linked with the experimentally observed functional effects of these inhibitors on allosteric regulation and substrate binding.

Prof. Vierling

July 26
Plant Cell Table of Contents for June 2016; Vol. 28, No. 6
Endosperm and Nucellus Develop Antagonistically in Arabidopsis Seeds
Wenjia Xu, Elisa Fiume, Olivier Coen, Christine Pechoux, Loïc Lepiniec, and Enrico Magnani
Plant Cell 2016 28: 1343-1360. First Published on May 27, 2016; doi:10.1105/tpc.16.00041
http://www.plantcell.org/content/28/6/1343.abstract
The endosperm and the nucellus develop antagonistically and in coordination with the seed coat through a signaling cascade that involves MADS box transcription factors and Polycomb-group proteins.

The Starch Granule-Associated Protein EARLY STARVATION1 Is Required for the Control of Starch Degradation in *Arabidopsis thaliana* Leaves
Doreen Feike, David Seung, Alexander Graf, Sylvain Bischof, Tamaryn Ellick, Mario Coiro, Sebastian Soyk, Simona Eicke, Tabea Mettler-Altmann, Kuan Jen Lu, Martin Trick, Samuel C. Zeeman, and Alison M. Smith
Plant Cell 2016 28: 1472-1489. First Published on May 20, 2016; doi:10.1105/tpc.16.00011
OPEN
http://www.plantcell.org/content/28/6/1472.abstract
Two proteins present in leaf starch granules are important for the control of starch turnover, allowing plants to match the depletion of starch reserves to the length of the night.

The Proteasome Stress Regulon Is Controlled by a Pair of NAC Transcription Factors in Arabidopsis
Nicholas P. Gladman, Richard S. Marshall, Kwang-Hee Lee, and Richard D. Vierstra
Plant Cell 2016 28: 1279-1296. First Published on May 18, 2016; doi:10.1105/tpc.15.01022
http://www.plantcell.org/content/28/6/1279.abstract
Proteotoxic stress in Arabidopsis is attenuated by a pair of NAC transcription factors that upregulate the synthesis of the 26S proteasome and other factors that promote protein homeostasis.

Nature Biotechnology Contents: Volume 34 pp 673 - 784
A bright cyan-excitable orange fluorescent protein facilitates dual-emission microscopy and enhances bioluminescence imaging in vivo **pp760 - 767**
Jun Chu, Younghee Oh, Alex Sens, Niloufar Ataie, Hod Dana *et al.*
doi:10.1038/nbt.3550
In vivo imaging is facilitated by a bright, cyan-excitable orange fluorescent protein that is the basis of an improved bioluminescent protein.
A split horseradish peroxidase for the detection of intercellular protein-protein interactions and sensitive visualization of synapses **pp774 - 780**
Jeffrey D Martell, Masahito Yamagata, Thomas J Deerinck, Sebastien Phan, Carolyn G Kwa *et al.*
doi:10.1038/nbt.3563
Synapses can be detected with high sensitivity by a split reporter that visualizes intercellular protein-protein interactions.
Plant, Cell & Environment Content Alert (New Articles)
Biochemical Basis of Sulphenomics: How Protein Sulphenic Acids may be Stabilized by the Protein Microenvironment
P. Trost, S. Fermani, M. Calvaresi and M. Zaffagnini
Accepted manuscript online: 8 JUL 2016 02:15PM EST | DOI: 10.1111/pce.12791

This review highlights the importance of acidity and nucleophilicity of protein cysteine thiols in determining the rate of H_2O_2-mediated primary oxidation to sulphenic acids. The stability and reactivity of sulphenic acids is also investigated and it is found to be strictly correlated to the cysteine environment and are dependent upon structural determinants, which are specific of each protein sensitive to oxidation. These finding reinforces the prominent role of cysteine sulphenic acids in redox signaling but a combination of biochemical, structural and computational approaches is mandatory to get insight into the kinetic and thermodynamics factors influencing cysteine oxidation.

Science http://doi.org/bk5b (2016)

Poor nutrition during pregnancy stunts the growth of young mice by modifying their gene expression.

Michelle Holland and Vardhman Rakyan at Queen Mary University of London and their colleagues fed female mice diets containing either 8% or 20% protein throughout pregnancy and

until weaning. They analysed patterns of methylation — which can influence gene expression — on the DNA of the rodents' offspring.

Pups from mothers fed the low-protein diet were, on average, 25% smaller at weaning. This effect was further influenced by variation within an animal's many gene copies for ribosomes, the cell's protein-construction machines. The extent of growth restriction depended on the proportion an individual had of a particular gene variant.

Studying the effects of methylation and other chemical marks on ribosomal genes may shed light on some human diseases, the authors say.

Purification of plant complex protein extracts in non-denaturing conditions by in-solution isoelectric focusing
Pages 100-103 R.A. Ferreira, S. Martins-Dias

Donovan MR, Marr MT 2nd.
dFOXO Activates Large and Small Heat Shock Protein Genes in Response to Oxidative Stress to Maintain Proteostasis in Drosophila.
J Biol Chem. 2016 Jul 19;. [Epub ahead of print]
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Nature. 2016 Jun 21;534(7608):435-6. PMID: 27337301 [PubMed - indexed for MEDLINE]

Molecular Cell: Alert 16 July-22 July
eIF3 Peripheral Subunits Rearrangement after mRNA Binding and Start-Codon Recognition Original Research Article
Pages 206-217
A Small Molecule That Protects the Integrity of the Electron Transfer Chain Blocks the Mitochondrial Apoptotic Pathway Original Research Article
Pages 229-239
The Plant Journal Content Alert (New Articles)
Retrograde signalling caused by heritable mitochondrial dysfunction is partially mediated by ANAC017 and improves plant performance
Olivier Van Aken, Ethan Ford, Ryan Lister, Shaobai Huang and A. Harvey Millar
Accepted manuscript online: 18 JUL 2016 07:05AM EST | DOI: 10.1111/tpj.13276

Nat. Cell Biol. **18**, 765 (2016).
How cells take out the trash Stella M. Hurtley
Misfolded proteins are generally sequestered and then degraded by one of a number of quality-control pathways within cells. Lysosomal enzymes in the endolysosomal system or proteasomes in the cytosol can do this. Lee *et al.* describe a rather unexpected way that some cells, when subjected to proteasomal insufficiency, deal with misfolded cytosolic proteins: They excrete them using an unconventional secretory pathway. The pathway involves an endoplasmic reticulum (ER)–associated deubiquitination enzyme, USP19. Somehow USP19 recognizes misfolded cytosolic proteins and delivers them to ER-associated endosomes, which then seem to spit out the aberrant proteins into the medium. How important or widespread this pathway is in normal physiology or disease remains to be seen.

*Science*22 Jul 2016 : 389-394

Accurate design of megadalton-scale two-component icosahedral protein complexes
By Jacob B. Bale, Shane Gonen, Yuxi Liu, William Sheffler, Daniel Ellis, Chantz Thomas, Duilio Cascio, Todd O. Yeates, Tamir Gonen, Neil P. King, David Baker
Nature provides many examples of self- and co-assembling protein-based molecular machines, including icosahedral protein cages that serve as scaffolds, enzymes, and compartments for essential biochemical reactions and icosahedral virus capsids, which encapsidate and protect viral genomes and mediate entry into host cells. Inspired by these natural materials, we report the computational design and experimental characterization of co-assembling, two-component, 120-subunit icosahedral protein nanostructures with molecular weights (1.8 to 2.8 megadaltons) and dimensions (24 to 40 nanometers in diameter) comparable to those of small viral capsids. Electron microscopy, small-angle x-ray scattering, and x-ray crystallography show that 10 designs spanning three distinct icosahedral architectures form materials closely matching the design models. In vitro assembly of icosahedral complexes from independently purified components occurs rapidly, at rates comparable to those of viral capsids, and enables controlled packaging of molecular cargo through charge complementarity. The ability to design

megadalton-scale materials with atomic-level accuracy and controllable assembly opens the door to a new generation of genetically programmable protein-based molecular machines.

Cospeciation of gut microbiota with hominids
By Andrew H. Moeller, Alejandro Caro-Quintero, Deus Mjungu, Alexander V. Georgiev, Elizabeth V. Lonsdorf, Martin N. Muller, Anne E. Pusey, Martine Peeters, Beatrice H. Hahn, Howard Ochman
*Science*22 Jul 2016 : 380-382
Rapidly evolving *gyrB* gene sequences of gut microbes from humans, wild chimpanzees, bonobos, and gorillas show coevolution.

Cell http://dx.doi.org/10.1016/j.cell.2016.05.048 (2016)
Baldridge, R. D. & Rapoport T. A. Autoubiquitination of the Hrd1 ligase triggers protein retrotranslocation in ERAD. Hrd1 may form a channel regulated by autoubiquitylation that has a major role in translocating misfolded proteins from the ER lumen to the cytoplasm for subsequent degradation.

Nature Chemical Biology Contents: August 2016, Volume 12 No 8 pp 575 - 656
Chaperones: Speedy motion for function **pp576 - 577**
Hagen Hofmann doi:10.1038/nchembio.2130
Hsp90 is an energy-consuming molecular chaperone that activates oncogenic proteins in a complicated multi-step reaction. Photoinduced electron transfer (PET) quenching experiments with a fluorescent reporter have now identified molecular transitions at multiple timescales in the chaperone cycle of Hsp90.

Metabolism: A new layer of glycolysis **pp577 - 578**
Maria V Liberti and Jason W Locasale doi:10.1038/nchembio.2133
Glucose metabolism has long been thought to operate with exquisite specificity and near-optimal efficiency. New findings show, however, that two glycolytic enzymes produce minor products that inhibit other enzymes involved in central carbon metabolism unless they are further metabolized by a novel enzyme.