Lit Lunch: 10_31_14

1) Damian:

Plant Metabolic Modeling: Achieving New Insight into Metabolism and Metabolic Engineering
Kambiz Baghalian, Mohammad-Reza Hajirezaei, and Falk Schreiber
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http://www.plantcell.org/content/early/2014/10/24/tpc.114.130328.abstract

Indu:

1. Science. 2014 Oct 17;346(6207):360-3. doi: 10.1126/science.1253168.

   HSF-1-mediated cytoskeletal integrity determines thermotolerance and life span.

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   The conserved heat shock transcription factor-1 (HSF-1) is essential to cellular stress resistance and life-span determination. The canonical function of HSF-1 is to regulate a network of genes encoding molecular chaperones that protect proteins from damage caused by extrinsic environmental stress or intrinsic age-related deterioration. In Caenorhabditis elegans, we engineered a modified HSF-1 strain that increased stress resistance and longevity without enhanced chaperone induction. This health assurance acted through the regulation of the calcium-binding protein PAT-10. Loss of pat-10 caused a collapse of the actin cytoskeleton, stress resistance, and life span. Furthermore, overexpression of pat-10 increased actin filament stability, thermotolerance, and longevity, indicating that in addition to chaperone regulation, HSF-1 has a prominent role in cytoskeletal integrity, ensuring cellular function during stress and aging.

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   PMID: 25324391 [PubMed - in process]

2. Science. 2014 Oct 24;346(6208):1257998. doi: 10.1126/science.1257998. Epub 2014 Oct 23.

   Lattice light-sheet microscopy: imaging molecules to embryos at high spatiotemporal resolution.

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Although fluorescence microscopy provides a crucial window into the physiology of living specimens, many biological processes are too fragile, are too small, or occur too rapidly to see clearly with existing tools. We crafted ultrathin light sheets from two-dimensional optical lattices that allowed us to image three-dimensional (3D) dynamics for hundreds of volumes, often at subsecond intervals, at the diffraction limit and beyond. We applied this to systems spanning four orders of magnitude in space and time, including the diffusion of single transcription factor molecules in stem cell spheroids, the dynamic instability of mitotic microtubules, the immunological synapse, neutrophil motility in a 3D matrix, and embryogenesis in Caenorhabditis elegans and Drosophila melanogaster. The results provide a visceral reminder of the beauty and the complexity of living systems.

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3. Science. 2014 Oct 24;346(6208):473-7. doi: 10.1126/science.1257037.

Influenza A virus uses the aggresome processing machinery for host cell entry.

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Comment in
Science. 2014 Oct 24;346(6208):427-8.

During cell entry, capsids of incoming influenza A viruses (IAVs) must be uncoated before viral ribonucleoproteins (vRNPs) can enter the nucleus for replication. After hemagglutinin-mediated membrane fusion in late endocytic vacuoles, the vRNPs and the matrix proteins dissociate from each other and disperse within the cytosol. Here, we found that for capsid disassembly, IAV takes advantage of the host cell's aggresome formation and disassembly machinery. The capsids mimicked misfolded protein aggregates by carrying unanchored ubiquitin chains that activated a histone deacetylase 6 (HDAC6)-dependent pathway. The ubiquitin-binding domain was essential for recruitment of HDAC6 to viral fusion sites and for efficient uncoating and infection. That other components of the aggresome processing machinery, including dynein, dynactin, and myosin II, were also required suggested that physical forces generated by microtubule- and actin-associated motors are essential for IAV entry.

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PMID: 25342804 [PubMed - in process]

Nathen:

1) Conversion of a Chaperonin GroEL-Independent Protein into an Obligate Substrate.

Ishimoto T, Fujiwara K, Niwa T, Taguchi H.

Chaperones assist protein folding by preventing unproductive protein aggregation in the cell. In Escherichia coli, chaperonin GroEL/GroES (GroE) is the only indispensable chaperone and is absolutely required for the de novo folding of at least ~60 proteins. We previously found that several orthologs of the obligate GroE substrates in Ureaplasma urealyticum, which lacks the groE gene in the genome, are E. coli GroE-independent folders, despite their significant sequence identities. Here, we investigated the key features that define the GroE-dependency. Chimera or random mutagenesis analyses revealed that independent multiple point mutations, and even single mutations, were sufficient to confer GroE-dependence on the Ureaplasma MetK. Strikingly, the GroE-dependency was well correlated with the propensity to form protein aggregates during folding. The results reveal the delicate balance between GroE-dependence and independence. The function of GroE to buffering the aggregation-prone mutations plays a role in maintaining higher genetic diversity of proteins

2) A faster Rubisco with potential to increase photosynthesis in crops
Myat T. Lin, Alessandro Occhialini, P. John Andralojc, Martin A. J. Parry & Maureen R. Hanson

In photosynthetic organisms, D-ribulose-1,5-bisphosphate carboxylase/oxygenase (Rubisco) is the major enzyme assimilating atmospheric CO2 into the biosphere1. Owing to the wasteful oxygenase

activity and slow turnover of Rubisco, the enzyme is among the most important targets for improving the photosynthetic efficiency of vascular plants2, 3. It has been anticipated that introducing the CO2-concentrating mechanism (CCM) from cyanobacteria into plants could enhance crop yield4, 5, 6. However, the complex nature of Rubisco's assembly has made manipulation of the enzyme extremely challenging, and attempts to replace it in plants with the enzymes from cyanobacteria and red algae have not been successful7, 8. Here we report two transplastomic tobacco lines with functional Rubisco from the cyanobacterium Synechococcus elongatus PCC7942 (Se7942). We knocked out the native tobacco gene encoding the large subunit of Rubisco by inserting the large and small subunit genes of the Se7942 enzyme, in combination with either the corresponding Se7942 assembly chaperone, RbcX, or an internal carboxysomal protein, CcmM35, which incorporates three small subunit-like domains9, 10. Se7942 Rubisco and CcmM35 formed macromolecular complexes within the chloroplast stroma, mirroring an early step in the biogenesis of cyanobacterial β-carboxysomes11, 12. Both transformed lines were photosynthetically competent, supporting autotrophic growth, and their respective forms of Rubisco had higher rates of CO2 fixation per unit of enzyme than the tobacco control. These transplastomic tobacco lines represent an important step towards improved photosynthesis in plants and will be valuable hosts for future addition of the remaining components of the cyanobacterial CCM, such as inorganic carbon transporters and the β-carboxysome shell proteins4, 5, 6.

Keith:

1) Uncovering global SUMOylation signaling networks in a site-specific manner

Nature Structural & Molecular Biology 21, 927–936 (2014)

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◦ Rochelle C J D'Souza & Matthias Mann

SUMOylation is a reversible post-translational modification essential for genome stability. Using high-resolution MS, we have studied global SUMOylation in human cells in a site-specific manner, identifying a total of >4,300 SUMOylation sites in >1,600 proteins. To our knowledge, this is the first time that >1,000 SUMOylation sites have been identified under standard growth conditions. We quantitatively studied SUMOylation dynamics in response to SUMO protease inhibition,

proteasome inhibition and heat shock. Many SUMOylated lysines have previously been reported to be ubiquitinated, acetylated or methylated, thus indicating cross-talk between SUMO and other post-translational modifications. We identified 70 phosphorylation and four acetylation events in proximity to SUMOylation sites, and we provide evidence for acetylation-dependent SUMOylation of endogenous histone H3. SUMOylation regulates target proteins involved in all nuclear processes including transcription, DNA repair, chromatin remodeling, precursor-mRNA splicing and ribosome assembly.

2) Dissection of Structural and Functional Requirements That Underlie the Interaction of ERdj3 Protein with Substrates in the Endoplasmic Reticulum

Journal of Biological Chemistry, 289, 27504-27512.

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ERdj3, a mammalian endoplasmic reticulum (ER) Hsp40/DnaJ family member, binds unfolded proteins, transfers them to BiP, and concomitantly stimulates BiP ATPase activity. However, the requirements for ERdj3 binding to and release from substrates in cells are not well understood. We found that ERdj3 homodimers that cannot stimulate the ATPase activity of BiP (QPD mutants) bound to unfolded ER proteins under steady state conditions in much greater amounts than wild-type ERdj3. This was due to reduced release from these substrates as opposed to enhanced binding, although in both cases dimerization was strictly required for substrate binding. Conversely, heterodimers consisting of one wild-type and one

mutant ERdj3 subunit bound substrates at levels comparable with wild-type ERdj3 homodimers, demonstrating that release requires only one protomer to be functional in stimulating BiP ATPase activity. Co-expressing wild-type ERdj3 and a QPD mutant, which each exclusively formed homodimers, revealed that the release rate of wild-type ERdj3 varied according to the relative half-lives of substrates, suggesting that ERdj3 release is an important step in degradation of unfolded client proteins in the ER. Furthermore, pulse-chase experiments revealed that the binding of QPD mutant homodimers remained constant as opposed to increasing, suggesting that ERdj3 does not normally undergo reiterative binding cycles with substrates.

Stephanie:

1) An Evolutionarily Conserved Prion-like Element Converts Wild Fungi from Metabolic Specialists to Generalists

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[*GAR*+] is a protein-based element of inheritance that allows yeast (*Saccharomyces cerevisiae*) to circumvent a hallmark of their biology: extreme metabolic specialization for glucose fermentation. When glucose is present, yeast will not use other carbon sources. [*GAR*+] allows cells to circumvent this “glucose repression.” [*GAR*+] is induced in yeast by a factor secreted by bacteria inhabiting their environment. We report that de novo rates of [*GAR*+] appearance correlate with the yeast’s ecological niche. Evolutionarily distant fungi possess similar epigenetic elements that are also induced by bacteria. As expected for a mechanism whose adaptive value originates from the selective pressures of life in biological communities, the ability of bacteria to induce [*GAR*+] and the ability of yeast to respond to bacterial signals have been extinguished repeatedly during the extended monoculture of domestication. Thus, [*GAR*+] is a broadly conserved adaptive strategy that links environmental and social cues to heritable changes in metabolism.