Lit Lunch 1/23/15

**Stephanie:**

Plant Mol Biol. 2015 Feb;87(3):303-15. doi: 10.1007/s11103-014-0277-7. Epub 2014 Dec 24.

**Arabidopsis thaliana thymidine kinase 1a is ubiquitously expressed during development and contributes to confer tolerance to genotoxic stress.**

Pedroza-García JA1, Nájera-Martínez M, de la Paz Sanchez M, Plasencia J.
Author information

Abstract
Thymidine kinase catalyzes the first step in the nucleotide salvage pathway by transferring a phosphate group to a thymidine molecule. In mammals thymidine kinase supplies deoxyribonucleotides for DNA replication and DNA repair, and the expression of the gene is tightly regulated during the cell cycle. Although this gene is phylogenetically conserved in many taxa, its physiological function in plants remains unknown. The genome of the model plant Arabidopsis thaliana has two thymidine kinase genes (AtTK1a and AtTK1b) and microarray data suggest they might have redundant roles. In this study we analyzed the TK1a function by evaluating its expression pattern during development and in response to genotoxic stress. We also studied its role in DNA repair by the characterization of a mutant that contained the T-DNA insertion in the promoter region of the TK1a gene. We found that TK1a is expressed in most tissues during plant development and it was differentially induced by ultraviolet-C radiation because TK1b expression was unaffected. In the mutant, the T-DNA insertion caused a 40 % rise in transcript levels and enzyme activity in Arabidopsis seedlings compared to wild-type plants. This elevation was enough to confer tolerance to ultraviolet-C irradiation in dark conditions, as determined by root growth, and meristem length and structure. TK1a overexpression also provided tolerance to genotoxins that induce double-strand break. Our results suggest that thymidine kinase contributes to several DNA repair pathways by providing deoxythymidine triphosphate that serve as precursors for DNA repair and to balance deoxyribonucleotides pools.

**Nathen:**

**The proteome and lipidome of Synechocystis sp. PCC 6803 cells grown under light-activated heterotrophic conditions**

Nicole Plohnke1, Tobias Seidel2, Uwe Kahmann3, Matthias Rögner1, Dirk Schneider2 and Sascha Rexroth1

Cyanobacteria are photoautotrophic prokaryotes with a plant-like photosynthetic machinery. Due to their short generation times, the ease of their genetic manipulation, and the limited size of their genome and proteome, cyanobacteria are popular model

organisms for photosynthetic research. Although the principal mechanisms of photosynthesis are well-known, much less is known about the biogenesis of the thylakoid membrane, hosting the components of the photosynthetic and respiratory electron transport chain in cyanobacteria. Here we present a detailed proteome analysis of the important model and host organism Synechocystis sp. PCC 6803 under light-activated heterotrophic growth conditions. Due to the mechanistic importance and severe changes in thylakoid membrane morphology under light-activated heterotrophic growth conditions, a focus was put on the analysis of the membrane proteome, which is supported with a targeted lipidome analysis. In total, 1528 proteins (24.5 % membrane integral) were identified in our analysis. For 641 of these proteins quantitative information was obtained by spectral counting. Prominent changes are observed for proteins associated with oxidative stress response and protein folding. Due to the heterotrophic growth conditions, also proteins involved in carbon metabolism and C/N-balance were severely affected. Although intracellular thylakoid membranes were significantly reduced, only minor changes were observed in their protein composition. The increased proportion of the membrane-stabilizing sulfoqinovosyl diacyl lipids found in the lipidome analysis, as well as the increased content of lipids with more saturated acyl chains, are clear indications for a coordinated synthesis of proteins and lipids, resulting in stabilization of intracellular thylakoid membranes under stress conditions.

**Minsoo:**

1. J Inherit Metab Dis. 2015 Jan 18. [Epub ahead of print]

**Bi-allelic CLPB mutations cause cataract, renal cysts, nephrocalcinosis and 3-methylglutaconic aciduria, a novel disorder of mitochondrial protein disaggregation.**

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**Whole exome sequencing** was used to investigate **the genetic cause of mitochondrial disease** in two siblings with a syndrome of congenital lamellar cataracts associated with nephrocalcinosis, medullary cysts and 3-methylglutaconic aciduria. Autosomal recessive inheritance in a gene encoding a mitochondrially targeted protein was assumed; **the only variants which satisfied these criteria were c.1882C>T (p.Arg628Cys) and c.1915G>A (p.Glu639Lys) in the CLPB gene**, encoding a heat shock protein/chaperonin responsible for disaggregating mitochondrial and cytosolic proteins. Functional studies, including quantitative PCR (qPCR) and Western blot, support pathogenicity of these mutations. Furthermore, molecular modelling suggests that **the mutations disrupt interactions between subunits so that the CLPB hexamer cannot form or is unstable**, thus impairing its role as a protein disaggregase. We conclude that accumulation of protein aggregates underlies the development of cataracts and nephrocalcinosis in CLPB deficiency, which is a novel genetic cause of 3-methylglutaconic aciduria. A

**common mitochondrial cause for 3-methylglutaconic aciduria appears to be disruption of the architecture of the mitochondrial membranes**, as in Barth syndrome (tafazzin deficiency), Sengers syndrome (acylglycerol kinase deficiency) and MEGDEL syndrome (impaired remodelling of the mitochondrial membrane lipids because of SERAC1 mutations). We now propose that **perturbation of the mitochondrial membranes by abnormal protein aggregates leads to 3-methylglutaconic aciduria in CLPB deficiency.**

**Mitochondrial ClpB-m mutant has no phenotype in arabidopsis.**

**Nature Plants**
**2. Regulatory uncertainty over genome editing**

Huw D. Jones

Nature Plants 1, Article number: 14011 (2015) ?doi:10.1038/nplants.2014.11
Published online 08 January 2015

Genome editing opens up opportunities for the precise and rapid alteration of crops to boost yields, protect against pests and diseases and enhance nutrient content. The extent to which applied plant research and crop breeding benefit will depend on how the EU decides to regulate this fledgling technology.

**ZFN, TALEN and CRISPR**
**USDA: plants containing targeted deletions generated by the cell's own repair mechanisms** do not fall under the umbrella of genetically modified organisms.
**European Union** considers an organism to be genetically modified if it has been altered in a way that does not occur **naturally by mating and/or natural recombination**. However, crops altered through **mutagenesis using chemicals and radiation are considered exempt** from these regulations. European Commission is yet to provide information on whether mutations made using site-directed nucleases also fall outside its regulatory criteria.

3. **Biochim Biophys Acta**. 2015 Jan 9. pii: S0005-2728(15)00002-X. doi: 10.1016/j.bbabio.2014.12.009. [Epub ahead of print]

**Emerging functions of mammalian and plant mTERFs.**

Kleine T(1), Leister D(2).

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Organellar gene expression (OGE) is crucial for plant development, respiration and photosynthesis, but the mechanisms that control it are still largely unclear. Thus, OGE requires various nucleus-encoded proteins that promote transcription, splicing, trimming and editing of organellar RNAs, and regulate their translation. In mammals, members of the mitochondrial transcription termination

factor (mTERF) family play important roles in OGE. Intriguingly, three of the four mammalian mTERFs do not actually terminate transcription, as their designation suggests, but appear to function in antisense transcription termination and ribosome biogenesis. During the evolution of land plants, the mTERF family has expanded to approximately 30 members, but knowledge of their function in photosynthetic organisms remains sparse. Here, we review **recent advances in the characterization of mterf mutants in mammals and photosynthetic organisms**, focusing particularly on the progress made in elucidating their molecular functions in the last two years.
**Shot1 mutant phenotype is similar to mammalian mterf4 mutant**

**Plant and Cell Physiology**
**4. Diffuse Decapping Enzyme DCP2 Accumulates in DCP1 Foci Under Heat Stress in Arabidopsis thaliana**
Kazuki Motomura1, Quy T.N. Le1, Takahiro Hamada1, Natsumaro Kutsuna2, Shoji Mano3,4, Mikio Nishimura3,4 and Yuichiro Watanabe1,*

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Abstract

2mRNAs. DCP2 is the catalytic core and DCP1 is an auxiliary subunit. It has been assumed that DCP1 and DCP2 are consistently co-localized in cytoplasmic RNA granules called processing bodies (P-bodies). However, it has not been confirmed whether DCP1 and DCP2 co-localize in Arabidopsis thaliana. In this study, we generated DCP1–green fluorescent protein (GFP) and DCP2–GFP transgenic plants that complemented dcp1 and dcp2 mutants, respectively, to see whether localization of DCP2 is identical to that of DCP1. DCP2 was present throughout the cytoplasm, whereas DCP1 formed P-body-like foci. Use of DCP1–GFP/DCP2–red fluorescent protein (RFP) or DCP1–RFP/DCP2–GFP plants showed that heat treatment induced DCP2 assembly into DCP1 foci. In contrast, cold treatment did not induce DCP2 assembly, while the number of DCP1 foci increased. These changes in DCP1 and DCP2 localization during heat and cold treatments occurred without changes in DCP1 and DCP2 protein abundance. Our results show that DCP1 and DCP2 respond differently to environmental changes, indicating that P-bodies have diverse DCP1 and DCP2 proportions depending on environmental conditions. The localization changes of DCP1 and DCP2 may explain how specific mRNAs are degraded during changes in environmental conditions.

**5. Whole-Genome Analysis of Herbicide-Tolerant Mutant Rice Generated by Agrobacterium-Mediated Gene Targeting**
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Abstract

**Gene targeting (GT) is a technique used to modify endogenous genes in target genomes precisely via homologous recombination (HR).** Although GT plants are produced using genetic transformation techniques, if the difference between the endogenous and the modified gene is limited to point mutations, GT crops can be considered equivalent to non-genetically modified mutant crops generated by conventional mutagenesis techniques. However, **it is difficult to guarantee the non-incorporation of DNA fragments from Agrobacterium in GT plants created by Agrobacterium-mediated GT** despite screening with conventional Southern blot and/or PCR techniques. Here, we report a comprehensive analysis of herbicide-tolerant rice plants generated by inducing point mutations in the rice ALS gene via Agrobacterium-mediated GT. **We performed genome comparative genomic hybridization (CGH) array analysis and whole-genome sequencing to evaluate the molecular composition of GT rice plants.** Thus far, **no integration of Agrobacterium-derived DNA fragments** has been detected in GT rice plants. However, **>1,000 single nucleotide polymorphisms (SNPs) and insertion/deletion (InDels) were found in GT plants**. Among these mutations, 20–100 variants might have some effect on expression levels and/or protein function. Information about additive mutations should be useful in clearing out unwanted mutations **by backcrossing**.

## Indu:

1. Science. 2015 Jan 2;347(6217):83-6. doi: 10.1126/science.1258857.

   Aging. Lysosomal signaling molecules regulate longevity in Caenorhabditis elegans.

   Folick A(1), Oakley HD(2), Yu Y(2), Armstrong EH(3), Kumari M(4), Sanor L(5), Moore DD(6), Ortlund EA(3), Zechner R(4), Wang MC(7).

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   Comment in
   Science. 2015 Jan 2;347(6217):32-3.

   Lysosomes are crucial cellular organelles for human health that function in digestion and recycling of extracellular and intracellular macromolecules. We describe a signaling role for lysosomes that affects aging. In the worm

Caenorhabditis elegans, the lysosomal acid lipase LIPL-4 triggered nuclear translocalization of a lysosomal lipid chaperone LBP-8, which promoted longevity by activating the nuclear hormone receptors NHR-49 and NHR-80. We used high-throughput metabolomic analysis to identify several lipids in which abundance was increased in worms constitutively overexpressing LIPL-4. Among them, oleoylethanolamide directly bound to LBP-8 and NHR-80 proteins, activated transcription of target genes of NHR-49 and NHR-80, and promoted longevity in C. elegans. These findings reveal a lysosome-to-nucleus signaling pathway that promotes longevity and suggest a function of lysosomes as signaling organelles in metazoans.



PMID: 25554789 [PubMed - indexed for MEDLINE]

2. Science. 2015 Jan 9;347(6218):1254806. doi: 10.1126/science.1254806. Epub 2014 Dec 18.

RNA splicing. The human splicing code reveals new insights into the genetic determinants of disease.

Xiong HY(1), Alipanahi B(1), Lee LJ(1), Bretschneider H(2), Merico D(3), Yuen RK(3), Hua Y(4), Gueroussov S(5), Najafabadi HS(1), Hughes TR(6), Morris Q(7), Barash Y(8), Krainer AR(4), Jojic N(9), Scherer SW(10), Blencowe BJ(11), Frey BJ(12).

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Comment in
Science. 2015 Jan 9;347(6218):124-5.

To facilitate precision medicine and whole-genome annotation, we developed a machine-learning technique that scores how strongly genetic variants affect RNA splicing, whose alteration contributes to many diseases. Analysis of more than 650,000 intronic and exonic variants revealed widespread patterns of mutation-driven aberrant splicing. Intronic disease mutations that are more than 30 nucleotides from any splice site alter splicing nine times as often as common variants, and missense exonic disease mutations that have the least impact on protein function are five times as likely as others to alter splicing. We detected tens of thousands of disease-causing mutations, including those involved in cancers and spinal muscular atrophy. Examination of intronic and exonic variants found using whole-genome sequencing of individuals with autism revealed misspliced genes with neurodevelopmental phenotypes. Our approach provides evidence for causal variants and should enable new discoveries in precision medicine.



PMID: 25525159 [PubMed - in process]

**Keith:**

## Journal of Biological Chemistry

## The H50Q Mutation Induces a 10-fold Decrease in the Solubility of α-Synuclein

## January 23, 2015 The Journal of Biological Chemistry, 290, 2395-2404.

**Riccardo Porcari‡, Christos Proukakis§, Christopher A. Waudby¶, Benedetta Bolognesi‖, P. Patrizia Mangione‡,**, Jack F. S. Paton¶, Stephen Mullin¶, Lisa D. Cabrita¶, Amanda Penco‡‡, Annalisa Relini‡‡, Guglielmo Verona‡,**, Michele Vendruscolo§§, Monica Stoppini**, Gian Gaetano Tartaglia‖, Carlo Camilloni§§, John Christodoulou¶1, Anthony H. V. Schapira§2 and Vittorio Bellotti‡,**3**

**‡Wolfson Drug Discovery Unit, Centre for Amyloidosis and Acute Phase Proteins, Division of Medicine, and the §Department of Clinical Neuroscience, Institute of Neurology, University College London, London NW3 2PF, United Kingdom, the ‖Centre for Genomic Regulation and University Pompeu Fabra, 08003 Barcelona, Spain, the **Department of Molecular Medicine, Institute of Biochemistry, University of Pavia, 27100 Pavia, Italy, the ¶Department of Structural and Molecular Biology, University College London, London WC1E 6BT, United Kingdom, the §§Department of Chemistry, University of Cambridge, Cambridge CB2 1EW, United Kingdom, and the ‡‡Department of Physics, University of Genoa, 16146 Genoa, Italy**

**Abstract**

**The conversion of α-synuclein from its intrinsically disordered monomeric state into the fibrillar cross-β aggregates characteristically present in Lewy bodies is largely unknown. The investigation of α-synuclein variants causative of familial forms of Parkinson disease can provide unique insights into the conditions that promote or inhibit aggregate formation. It has been shown recently that a newly identified pathogenic mutation of α-synuclein, H50Q, aggregates faster than the wild-type. We investigate here its aggregation propensity by using a sequence-based prediction algorithm, NMR chemical shift analysis of secondary structure populations in the monomeric state, and determination of thermodynamic stability of the fibrils. Our data show that the H50Q mutation induces only a small increment in polyproline II structure around the site of the mutation and a slight increase in the overall aggregation propensity. We also find, however, that the H50Q mutation strongly stabilizes α-synuclein fibrils by 5.0 ± 1.0 kJ mol−1, thus increasing the supersaturation of monomeric α-synuclein within the cell, and strongly favors its aggregation process. We further show that wild-type α-synuclein can decelerate the aggregation kinetics of the H50Q variant in a dose-dependent manner when coaggregating with it. These last findings suggest that the precise balance of α-synuclein synthesized from the wild-type and mutant alleles may influence the natural history and heterogeneous clinical phenotype of Parkinson disease.**

**Atypical Ubiquitylation in Yeast Targets Lysine-less Asi2 for Proteasomal Degradation**

**January 23, 2015 The Journal of Biological Chemistry, 290, 2489-2495.**

**Mirta Boban‡, Per O. Ljungdahl§ and Roland Foisner‡1**

**Max F. Perutz Laboratories, Department of Medical Biochemistry, Medical University Vienna, A-1030 Vienna, Austria and the §Department of Molecular Biosciences, Wenner-Gren Institute, Stockholm University SE-S-10691 Stockholm, Sweden**

**Abstract**

**Proteins are typically targeted for proteasomal degradation by the attachment of a polyubiquitin chain to ϵ-amino groups of lysine residues. Non-lysine ubiquitylation of proteasomal substrates has been considered an atypical and rare event limited to complex eukaryotes. Here we report that a fully functional lysine-less mutant of an inner nuclear membrane protein in yeast, Asi2, is polyubiquitylated and targeted for proteasomal degradation. Efficient degradation of lysine-free Asi2 requires E3-ligase Doa10 and E2 enzymes Ubc6 and Ubc7, components of the endoplasmic reticulum-associated degradation pathway. Together, our data suggest that non-lysine ubiquitylation may be more prevalent than currently considered.**

**Damian:**

**Cell**

**Ligand-Dependent Enhancer Activation Regulated by Topoisomerase-I Activity**

Janusz Puc, Piotr Kozbial, Wenbo Li, Yuliang Tan, Zhijie Liu, Tom Suter, Kenneth A. Ohgi, Jie Zhang, Aneel K. Aggarwal, Michael G. Rosenfeld
Published online: January 22, 2015

**Extracellular Metabolic Energetics Can Promote Cancer Progression**

Jia Min Loo, Alexis Scherl, Alexander Nguyen, Fung Ying Man, Ethan Weinberg, Zhaoshi Zeng, Leonard Saltz, Philip B. Paty, Sohail F. Tavazoie
Published online: January 15, 2015

**Elimination of Unfit Cells Maintains Tissue Health and Prolongs Lifespan**

Marisa M. Merino, Christa Rhiner, Jesus M. Lopez-Gay, David Buechel, Barbara Hauert, Eduardo Moreno
Published online: January 15, 2015

**Glial Lipid Droplets and ROS Induced by Mitochondrial Defects Promote Neurodegeneration**

Lucy Liu, Ke Zhang, Hector Sandoval, Shinya Yamamoto, Manish Jaiswal, Elisenda Sanz, Zhihong Li, Jessica Hui, Brett H. Graham, Albert Quintana, Hugo J. Bellen

Plant Physiology

- Amy R. Knobbe,
- Kempton M. Horken,
- Thomas M. Plucinak,
- **Eniko Balasssa Hakim,**

- **Heriberto Cerutti,**
- **and Donald P. Weeks**

**SUMOylation by a stress-specific SUMO E2 conjugase is essential for survival of Chlamydomonas reinhardtii under stress conditionsPlant Physiol. pp.114.256081;**

First Published on January 22, 2015;doi:10.1104/pp.114.256081

- Soo Min Park,
- Keun Pill Kim,
- Mi Chung Suh,
- Mi Ok Lee,
- Seong-Kon Lee,
- Xinli Xia,
- and Choo Bong Hong

**Small Heat Shock Proteins Can Release Light Dependence of Tobacco Seed During GerminationPlant Physiol. pp.114.252841; First Published on January 20, 2015;doi:10.1104/pp.114.252841**

- Shi Jianghua,
- Yi Keke,
- Liu Yu,
- Xie Li,
- Zhou Zhongjing,
- Chen Yue,
- Hu Zhanghua,
- Zheng Tao,
- Liu Renhu,
- Chen Yunlong,
- and Chen Jinqing

**Phosphoenolpyruvate Carboxylase in Arabidopsis Leaves Plays a Crucial Role in Carbon and Nitrogen MetabolismPlant Physiol. pp.114.254474; First Published on January 14, 2015;doi:10.1104/pp.114.254474**

**Plant Journal**

**Reactive oxygen species-provoked mitochondria-dependent cell death during ageing of elm (Ulmus pumila L.) seeds**
**Yu Wang, Ying Li, Hua Xue, Hugh W. Pritchard and Xiaofeng Wang**
**Article first published online: 14 JAN 2015 | DOI: 10.1111/tpj.12737**

**Fionn:**

**Nature**

**Endophilin marks and controls a clathrin-independent endocytic pathway**

Emmanuel Boucrot, Antonio P. A. Ferreira, Leonardo Almeida-Souza, Sylvain Debard, Yvonne Vallis, Gillian Howard, Laetitia Bertot, Nathalie Sauvonnet & Harvey T. McMahon

Endocytosis is required for internalization of micronutrients and turnover of membrane components. Endophilin has been assigned as a component of clathrin-mediated endocytosis. Here we show in mammalian cells that endophilin marks and controls a fast-acting tubulovesicular endocytic pathway that is independent of AP2 and clathrin, activated upon ligand binding to cargo receptors, inhibited by inhibitors of dynamin, Rac, phosphatidylinositol-3-OH kinase, PAK1 and actin polymerization, and activated upon Cdc42 inhibition. This pathway is prominent at the leading edges of cells where phosphatidylinositol-3,4-bisphosphate?produced by the dephosphorylation of phosphatidylinositol-3,4,5-triphosphate by SHIP1 and SHIP2?recruits lamellipodin, which in turn engages endophilin. This pathway mediates the ligand-triggered uptake of several G-protein-coupled receptors such as ?2a- and ?1-adrenergic, dopaminergic D3 and D4 receptors and muscarinic acetylcholine receptor 4, the receptor tyrosine kinases EGFR, HGFR, VEGFR, PDGFR, NGFR and IGF1R, as well as interleukin-2 receptor. We call this new endocytic route fast endophilin-mediated endocytosis (FEME).

**Productivity limits and potentials of the principles of conservation agriculture**

Cameron M. Pittelkow, Xinqiang Liang, Bruce A. Linquist, Kees Jan van Groenigen, Juhwan Lee, Mark E. Lundy, Natasja van Gestel, Johan Six, Rodney T. Venterea & Chris van Kessel

One of the primary challenges of our time is to feed a growing and more demanding world population with reduced external inputs and minimal environmental impacts, all under more variable and extreme climate conditions in the future1, 2, 3, 4. Conservation agriculture represents a set of three crop management principles that has received strong international support to help address this challenge5, 6, with recent conservation agriculture efforts focusing on smallholder farming systems in sub-Saharan Africa and South Asia7. However, conservation agriculture is highly debated, with respect to both its effects on crop yields8, 9, 10 and its applicability in different farming contexts7, 11, 12, 13. Here we conduct a global meta-analysis using 5,463 paired yield observations from 610 studies to compare no-till, the original and central concept of conservation agriculture, with conventional tillage practices across 48 crops and 63 countries. Overall, our results show that no-till reduces yields, yet this response is variable and under certain conditions no-till can produce equivalent or greater yields than conventional tillage. Importantly, when no-till is combined with the other two conservation agriculture principles of residue retention and crop rotation, its negative impacts are minimized.

Moreover, no-till in combination with the other two principles significantly increases rainfed crop productivity in dry climates, suggesting that it may become an important climate-change adaptation strategy for ever-drier regions of the world. However, any expansion of conservation agriculture should be done with caution in these areas, as implementation of the other two principles is often challenging in resource-poor and vulnerable smallholder farming systems, thereby increasing the likelihood of yield losses rather than gains. Although farming systems are multifunctional, and environmental and socio-economic factors need to be considered14, 15, 16, our analysis indicates that the potential contribution of no-till to the sustainable intensification of agriculture is more limited than often assumed.