PNAS Plus Significance Statements

Crossover from band-like to thermally activated charge transport in organic transistors due to strain-induced traps

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The operation of organic field-effect transistors is governed by the processes taking place at the device interfaces. The mismatch in the coefficients of thermal expansion of the consecutive layers can induce inhomogeneous strain in the organic semiconductor layer and reduce performance by increasing the electronic trap density. We show that a high-quality organic semiconductor layer is necessary, but not sufficient, to obtain efficient charge-carrier transport, and we propose a device design strategy that allows us to achieve the intrinsic performance limits of a given organic semiconductor regardless of the relative thermal expansions of the constituent layers. (See pp. E6739–E6748.)

Quantitative time-resolved chemoproteomics reveals that stable *O*-GlcNAc regulates box C/D snoRNP biogenesis

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In mammalian cells, more than 1,000 intracellular proteins are posttranslationally modified with *O*-linked GlcNAc (*O*-GlcNAc), which regulates many important biological processes. The *O*-GlcNAc modification has been found to dynamically cycle on and off the modified proteins. How *O*-GlcNAc affects protein stability remains to be investigated at the proteome level. In this work, we developed a quantitative time-resolved proteomic strategy to analyze the turnover dynamics of *O*-GlcNAcylated proteins. We discovered that not all protein *O*-GlcNAcylation events were reversible and that a subset of *O*-GlcNAcylated proteins exhibited minimal removal of *O*-GlcNAc or degradation of protein backbones. Our work reveals stable *O*-GlcNAc as an important regulatory mechanism for stabilizing proteins, such as core proteins of box C/D small nucleolar ribonucleoprotein complexes. (See pp. E6749–E6758.)

Impact of glacial/interglacial sea level change on the ocean nitrogen cycle

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Biologically available nitrogen (fixed N) limits the fertility of much of the ocean. Of the processes that remove fixed N from the ocean, conversion to N_2 in coastal sediments appears to dominate. This work provides the strongest data-based support for the long-standing hypothesis of changes in N loss along the ocean margin due to the cyclic drowning and emergence of the continental shelves. The data also imply strong local coupling of N loss to N_2 fixation, the dominant N input to the ocean, thus suggesting a stable oceanic fixed N reservoir over glacial cycles. Finally, this work points to glacial/interglacial oscillations in the biogeochemical fluxes at and near the ocean margins that would have influenced the evolution of coastal species. (See pp. E6759–E6766.)

Factor-dependent archaeal transcription termination

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Proper transcription regulation is necessary for timely and accurate gene expression underlying growth and development. Transcription is regulated at each stage of the transcription cycle—initiation, elongation, and termination—and it is critical to define the factors and sequences regulating RNA polymerase activity. Many studies have investigated the mechanisms used by transcription factors involved in regulation of transcription initiation and elongation, but a mechanistic understanding of transcription termination has been slower to emerge. Here we characterize the first archaeal transcription termination factor, termed euryarchaeal termination activity (Eta). The mechanisms of Eta-mediated termination provide the first understanding of archaeal factor-dependent termination and provide insight into and contrast with the mechanisms used for factor-dependent termination in extant life. (See pp. E6767–E6773.)

Conformational and chemical selection by a *trans*-acting editing domain

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Charging of tRNAs with the wrong amino acid can result in mistranslation of protein-encoding genes. Proofreading by tRNA editing domains clears these mischarged tRNAs, ensuring fidelity; however, structures of complexes with mischarged substrates are not currently available, and many mechanistic questions remain unanswered. ProXp-ala, present in all domains of life, selectively removes Ala from $tRNA^{Pro}$, leaving the cognate Pro-$tRNA^{Pro}$ intact. A chemically synthesized nonhydrolyzable substrate analog has allowed characterization of the enzyme-substrate complex using

NMR spectroscopy. Based on NMR studies, mutagenesis, enzymatic assays, molecular dynamics, and X-ray crystallography, we conclude that ProXp-ala uses multiple strategies, including conformational selection by a dynamic helix, size exclusion, and chemical discrimination, to ensure editing solely of Ala-tRNA^{Pro}. (See pp. E6774–E6783.)

Phospholipase A activity of adenylate cyclase toxin mediates translocation of its adenylate cyclase domain

David González-Bullón, Kepa B. Uribe, César Martín, and Helena Ostolaza

Numerous bacterial toxins can cross cell membranes, penetrating the cytosol of their target cells, but to do so exploits cellular endocytosis or intracellular sorting machineries. *Bordetella pertussis* adenylate cyclase toxin (ACT) delivers its catalytic domain directly across the cell membrane by an unknown mechanism, and generates cAMP, which subverts the cell signaling. Here, we decipher the fundamentals of the molecular mechanism of ACT transport. We find that AC translocation and, consequently cytotoxicity, are determined by an intrinsic ACT–phospholipase A (PLA) activity, supporting a model in which in situ generation of nonlamellar lysophospholipids by ACT–PLA activity remodels the cell membrane, forming proteolipidic toroidal "holes" through which AC domain transfer may directly take place. PLA-based specific protein transport in cells is unprecedented. (See pp. E6784–E6793.)

Homeostatic enhancement of sensory transduction

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How do biological systems ensure robustness of function despite developmental and environmental variation? Although the operation of some systems appears to require precise control over parameter values, we describe how the function of the ear might instead be made robust to parameter perturbation. The sensory hair cells of the cochlea are physiologically vulnerable, yet most ears remain highly sensitive despite differences in their physical properties.We propose that slow homeostatic feedback allows hair cells to detect weak acoustic signals over a wide span of parameter values. Homeostasis also ensures that hair cells exhibit sharp frequency selectivity and a broad dynamic range. This homeostatic strategy constitutes a general principle by which many biological systems might ensure robustness of function. (See pp. E6794–E6803.)

Time-resolved observation of protein allosteric communication

Sebastian Buchenberg, Florian Sittel, and Gerhard Stock

Allostery describes the puzzling phenomenon of long-range communication between distant protein sites. Representing the elementary process of cell signaling, allosteric interactions also provide prime targets in pharmaceutical research. Although a number of thermodynamic models have been proposed, the dynamic process of allosteric communication itself is still not well understood. Accounting for recent timeresolved infrared spectroscopy experiments, this study uses extensive all-atom molecular dynamics simulations that envision a real-time picture of the way allostery works. Mediated by the propagation of stress, allostery is found to trigger structural and dynamical changes in a nonlinear and nonlocal fashion. Similarly as found for downhill folding, the hierarchy and exceeding structural heterogeneity of the process gives rise to strongly nonexponential kinetics. (See pp. E6804–E6811.)

Oligomerization of the tetramerization domain of p53 probed by two- and three-color single-molecule FRET

Hoi Sung Chung, Fanjie Meng, Jae-Yeol Kim, Kevin McHale, Irina V. Gopich, and John M. Louis

Intrinsically disordered proteins often form pathological oligomers implicated in various diseases. In many cases, these oligomers cannot be separated and characterizations of their sizes and conformations are difficult. We develop a single-molecule fluorescence method that can probe individual oligomers without separation and determine the equilibrium constants and oligomerization kinetics. By combining two- and three-color single-molecule FRET spectroscopy with fluorescence lifetime analysis, it is possible to determine conformations and flexibility of individual oligomers unambiguously. We apply this method to the oligomerization of the tetramerization domain of p53 and compare conformations of monomer, dimer, and tetramer. This method will be useful in exploring other protein oligomerization systems involved in important biological and disease processes. (See pp. E6812–E6821.)

Exploiting conformational plasticity in the AAA+ protein VCP/p97 to modify function

Anne Kathrin Schütz, Enrico Rennella, and Lewis E. Kay

Cdc48/TERA/p97/VCP is an enzyme that utilizes energy stored in ATP to coordinate protein degradation and recycling in eukaryotic cells. Point mutations in p97 cause a degenerative disease in humans that affects the central nervous system, bone, and muscle. These mutations deregulate the structure and dynamics of p97 with implications for binding of a cofactor that recruits p97 to the lysosomal degradation pathway. Here we probe the plasticity of p97, searching for hotspots in this enzyme to revert the effect of disease mutations. We demonstrate that mutations at secondary sites can shift the dynamics and structure toward wild type, highlighting the potential of exploiting the plasticity of p97 in the rational design of compounds that restore function in disease mutants. (See pp. E6822–E6829.)

Intraflagellar transport velocity is governed by the number of active KIF17 and KIF3AB motors and their motility properties under load

Bojan Milic, Johan O. L. Andreasson, Daniel W. Hogan, and Steven M. Block

Intraflagellar transport (IFT)—cargo transport inside cilia—is mediated by two different kinesin-2 motors: the slower KIF3AB and the faster KIF17. It was not understood how ciliary cargos, called IFT trains, could attain velocities that exceed the unloaded rate of KIF3AB. We find that high IFT velocities cannot be explained by KIF3AB motors speeding up in response to being pulled forward by their KIF17 partners. Instead, IFT velocity is governed by an equilibrium between a slower state, where at least one KIF3AB motor on the train is actively participating in transport, and a faster state, where KIF3AB motors disengage, and only KIF17 motors ferry the train. The more often IFT trains access the faster state, the higher their overall velocity. (See pp. E6830–E6838.)

Testing inhomogeneous solvation theory in structure-based ligand discovery

Trent E. Balius, Marcus Fischer, Reed M. Stein, Thomas B. Adler, Crystal N. Nguyen, Anthony Cruz, Michael K. Gilson, Tom Kurtzman, and Brian K. Shoichet

Water molecules play a crucial role in protein–ligand binding. Calculating the energetic consequences of displacing water upon ligand binding has challenged the field for many years. Inhomogeneous solvation theory (IST) is one of the most popular methods for distinguishing favorable from unfavorable water molecules, but little controlled, prospective testing at atomic resolution has been done to evaluate the method. Here we compare molecular docking screens with and without an IST term to gauge its impact on ligand discovery. We test prospective ligand-binding predictions that include an IST term, using crystallography and direct binding. (See pp. E6839–E6846.)

Poly(ADP-ribose) polymerase 1 escorts XPC to UV-induced DNA lesions during nucleotide excision repair

Mihaela Robu, Rashmi G. Shah, Nupur K. Purohit, Pengbo Zhou, Hanspeter Naegeli, and Girish M. Shah

Repair of the majority of UV-induced DNA damage in mammalian cells by the nucleotide excision repair pathway starts with rapid recruitment of Xeroderma pigmentosum C (XPC) protein to the lesion. However, rapidity of XPC recruitment to the lesion site in a genomic context cannot be fully explained by the known properties of XPC or its partner protein DDB2. Here, we show that the DNA damage-detecting nuclear protein PARP1 forms a stable complex with XPC before DNA damage and transfers it very rapidly to the DNA lesion site if other repair conditions are present. Since PARP1 is known to interact with many proteins under steady-state conditions, our results reveal a paradigm that an association with PARP1 could confer a functional advantage to these proteins. (See pp. E6847–E6856.)

Superresolution expansion microscopy reveals the three-dimensional organization of the *Drosophila* synaptonemal complex

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Because inaccurate chromosome segregation during meiosis is a leading cause of miscarriage in humans, we seek to understand how homologous chromosomes segregate properly. Meiotic chromosome segregation occurs with fidelity only in the presence of the synaptonemal complex (SC), a protein structure that assembles between homologs and facilitates the occurrence of crossing over. Although some functions of the SC are evolutionarily conserved, the mechanisms underlying its multiple roles during meiosis, as well as organizational variances among different organisms, remain under investigation. Here we combine superresolution and expansion microscopy and find strong evidence that the *Drosophila* SC comprises two visually distinct layers, perhaps suggesting that each layer connects one sister chromatid from each homologous chromosome. (See pp. E6857–E6866.)

Interferon-γ is a master checkpoint regulator of cytokine-induced differentiation

Zhao Zha, Felicitas Bucher, Anahita Nejatfard, Tianqing Zheng, Hongkai Zhang, Kyungmoo Yea, and Richard A. Lerner

The understanding of the molecular mechanisms of activation and checkpoint processes has important therapeutic implications. Here, we show that interferon-γ is a master checkpoint regulator for many cytokines. It operates partially by activating STAT1 signaling. However, most important is the mechanism that allows it to assume master regulator status. To do this, it induces internalization of gp130, a common component of many heterodimeric cytokine receptors. Therefore, this cytokine checkpoint could open a whole new paradigm in cell biology. (See pp. E6867–E6874.)

DNA damage tolerance in hematopoietic stem and progenitor cells in mice

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The DNA damage response entails both DNA repair and DNA damage tolerance (DDT). DDT enables replicative bypass of fork-stalling DNA lesions and structures. Although DNA repair is known to be key in maintaining stem cells and tissue homeostasis, the contribution of DDT in stem cell maintenance remained to be defined. Using DDT-deficient $Pcna^{K164R/K164R}$ mice we here reveal a critical role of DDT in maintaining hematopoietic stem cells (HSCs). Defective DDT results in progressive impairment of HSCs, identifying DDT as a key player in preserving HSC fitness and prohibiting premature aging. (See pp. E6875–E6883.)

Elevated auxin biosynthesis and transport underlie high vein density in C_4 leaves

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Elevated leaf vein density is a key step in the evolution from C_3 to C_4 plants. We hypothesized that high vein density in C_4 leaves is due to elevated auxin biosynthesis and transport in developing leaves. We found higher expression levels of genes promoting auxin biosynthesis and higher auxin content in developing C_4 leaves than in developing C_3 leaves. We also found higher auxin content and vein density in loss-of-function mutants of *MYC2*, an auxin biosynthesis suppressor. Moreover, treatment with an auxin biosynthesis or transport inhibitor reduced vein density in new leaves. Finally, mutations that reduce auxin efflux or influx reduce vein density. These observations support our hypothesis and provide a molecular basis for high vein density in C_4 leaves. (See pp. E6884–E6891.)

IL-4–secreting eosinophils promote endometrial stromal cell proliferation and prevent *Chlamydia*-induced upper genital tract damage

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Chlamydia trachomatis is the most common sexually transmitted bacterium, but most genital infections in women are asymptomatic. Consistent with this presentation, *Chlamydia* ascension into human endometrial tissue elicits robust innate and adaptive type 2 immunity. Herein, we genitally infected mice with *C. trachomatis* to explore the significance of type 2 innate immunity, finding that IL-4–secreting eosinophils promote endometrial stromal cell proliferation and prevent *Chlamydia* infection from triggering upper genital tract tissue destruction. Such results identify eosinophils as essential for repairing murine genital tissue repair after infectious insult. They also identify a

need to define roles played by eosinophils in genital infections of women, and their role in other events associated with endometrial repair, including menstruation, endometritis, and endometriosis. (See pp. E6892–E6901.)

PUM1 is a biphasic negative regulator of innate immunity genes by suppressing LGP2

Yonghong Liu, Linlin Qu, Yuanyuan Liu, Bernard Roizman, and Grace Guoying Zhou

We report that PUM1, a protein linked to control of translation of mRNAs carrying a cognate sequence, is a negative regulator of LGP2. In turn LGP2 emerged as a biphasic master activator of numerous innate immunity genes leading to production of interferon. The studies traced in real-time the changes in innate immune responses following transfection of siPUM1 RNA. This approach enabled the discovery that innate immune genes analyzed in this report were activated sequentially in a cascade fashion. The studies were done in uninfected cells in the absence of viral gene products that could affect the expression of cellular genes. This report seeds the possibility of systemic engagement of innate immune responses following life-threatening viral infections by suppressing PUM1 function. (See pp. E6902–E6911.)

CD318 is a ligand for CD6

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The CD6 T cell surface glycoprotein regulates T cell activation, and *CD6* is a risk gene for autoimmune diseases including multiple sclerosis (MS). Moreover, recent work indicates that CD6 is an attractive target for the development of new therapeutic approaches to autoimmune diseases such as MS. The known ligand of CD6 is CD166 (also termed ALCAM), but CD6–CD166 interactions neither explain CD6-dependent interactions with stromal cell lineages that are critical in organ-targeted autoimmune diseases nor account for effects of CD6-targeted therapeutics in autoimmune diseases. This report definitively establishes CD318 as a second ligand of CD6 and provides evidence for the importance of CD6–CD318 interactions in autoimmune diseases that affect the central nervous system and the synovial lining of joints. (See pp. E6912–E6921.)

Escherichia coli cytochrome *c* peroxidase is a respiratory oxidase that enables the use of hydrogen peroxide as a terminal electron acceptor

Maryam Khademian and James A. Imlay

Hydrogen peroxide has been regarded exclusively as a hazard for bacteria; its sources and concentrations in natural habitats are uncertain. The cytochrome *c* peroxidase of *Escherichia coli* exhibits an expression pattern and flux rate that provides surprising insights into these issues. This periplasmic enzyme is induced only when H_2O_2 is present and molecular oxygen is absent. Intriguingly, it was ineffective as a defensive enzyme, but through its linkage to the quinone pool it did enable *E. coli* to respire using H_2O_2 as an anaerobic electron acceptor. We suggest that both chemical and biotic processes generate micromolar H_2O_2 at oxic/anoxic interfaces and that this scenario is common enough that microbes have evolved strategies to productively exploit the H_2O_2. (See pp. E6922–E6931.)

Distinct functions of diaphanous-related formins regulate HIV-1 uncoating and transport

Michael Keegan Delaney, Viacheslav Malikov, Qingqing Chai, Guangyuan Zhao, and Mojgan H. Naghavi

Viruses are adept at exploiting the host cytoskeleton to facilitate various aspects of their replication. Among host cytoskeletal regulators, diaphanous-related formins (DRFs) coordinate actin nucleation and microtubule (MT) stabilization in response to various environmental signals. Here, we uncover a function of DRFs and show that human immunodeficiency virus type 1 (HIV-1) exploits DRFs to coordinate the disassembly of the viral capsid shell, or "uncoating," with induction of MT stabilization and virus transport. These two functions of DRFs during HIV-1 infection were genetically separable and independent of actin. Our findings suggest that HIV-1 coopts discrete functions of DRFs to coordinately control uncoating and MT-based virus transport, mimicking how DRFs naturally function to coordinate host actin and MT dynamics. (See pp. E6932–E6941.)

Structural basis of subunit selectivity for competitive NMDA receptor antagonists with preference for GluN2A over GluN2B subunits

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Despite decades of studies, the development of competitive glutamate-site antagonists that can distinguish between NMDA receptor subtypes based on GluN2 subunits has been unsuccessful. The resulting lack of subunit-selective NMDA receptor ligands has led to the widespread use of competitive antagonists with only modest subunit preference in neurophysiological and behavioral studies. This study describes competitive glutamate-site antagonists with a binding mode in the GluN2A agonist binding domain that enables indirect engagement between ligands and nonconserved residues to achieve preferential binding to GluN1/2A over GluN1/2B. These findings are required for rational drug design and suggest that glutamate-site competitive antagonists with considerable subunit selectivity can be developed, despite the highly conserved nature of the glutamate binding site. (See pp. E6942–E6951.)

Neuronal cytoskeletal gene dysregulation and mechanical hypersensitivity in a rat model of Rett syndrome

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Cutaneous sensitivity appears to be abnormal in Rett syndrome and other autistic disorders. Using rats with disrupted methyl-CpG binding protein 2 (MeCP2) expression characteristic of Rett syndrome, we found that MeCP2 deficiency in sensory neurons led to augmented pressure and cold sensitivity but hyposensitivity to heat, accompanied by respective changes in cutaneous innervation. Transcriptome analysis of MeCP2-deficient ganglia showed up-regulation of genes associated with actin cytoskeletal dynamics and adhesion formation; down-regulating key genes in vivo normalized both

mechanical sensitivity and innervation density. These findings provide evidence that ganglion cytoskeletal genes play key roles in determining mechanosensory properties, which may contribute to altered pain sensitivity in Rett syndrome and other painful conditions. (See pp. E6952–E6961.)

Loss of clusterin shifts amyloid deposition to the cerebrovasculature via disruption of perivascular drainage pathways

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Deposition of amyloid-β (Aβ) peptide in the form of parenchymal plaques and Aβ accumulation in the walls of cerebral vessels as cerebral amyloid angiopathy (CAA) are pathological hallmarks of Alzheimer's disease (AD). The clusterin (*CLU*) gene, which confers AD risk, is associated with amyloid deposition. Here we show that loss of CLU promotes cerebrovascular CAA, yet significantly reduces the amount of parenchymal plaques by altering perivascular drainage of Aβ in the APP/PS1 mouse model of AD. The absence of CLU in these mice is associated with a lower number of hemorrhages and a decrease in inflammation. These results suggest that CLU functions as a major Aβ chaperone to maintain Aβ solubility along interstitial fluid drainage pathways and prevent CAA formation. (See pp. E6962–E6971.)

Low-frequency hippocampal–cortical activity drives brain-wide resting-state functional MRI connectivity

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The hippocampus with its dense reciprocal axonal projections to and from cortex is widely believed to mediate numerous cognitive functions. However, it is unknown whether and how specific hippocampal–cortical activity contributes to the brain-wide functional connectivity. Here, we use optogenetics and fMRI to examine how excitatory neural activity initiated in the dorsal dentate gyrus of the hippocampus propagates and modulates resting-state fMRI (rsfMRI) connectivity. We discover its robust propagation brain-wide at low frequency (1 Hz), which enhances interhemispheric rsfMRI connectivity and cortical and subcortical visual responses. Our findings highlight the important role of slow hippocampal–cortical oscillatory activity in driving brain-wide rsfMRI connectivity and mediating sensory processing. (See pp. E6972–E6981.)

Hyperpolarized ^{13}C MR metabolic imaging can detect neuroinflammation in vivo in a multiple sclerosis murine model

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Cells from the innate immune system, namely microglia and macrophages (mononuclear phagocytes, MPs), play a central role in the progression of neurological disorders such as multiple sclerosis. Such cells can contribute to lesion formations (proinflammatory) or participate in remyelinating processes (neuroprotective). When differentiated to a proinflammatory phenotype, MPs experience metabolic reprogramming leading to increased glycolysis and production of lactate. In this study we showed that a new metabolic imaging method, namely ^{13}C magnetic resonance spectroscopic imaging (MRSI) of hyperpolarized pyruvate, can detect increased lactate production from proinflammatory MPs, a mechanism mediated by pyruvate dehydrogenase kinase 1 upregulation, in a preclinical model of multiple sclerosis. These findings validate the potential of ^{13}C MRSI of hyperpolarized pyruvate for in vivo detection of neuroinflammation. (See pp. E6982–E6991.)

Cdk5-dependent phosphorylation of liprinα1 mediates neuronal activity-dependent synapse development

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The activity-dependent organization of synaptic components occurs during brain development in response to experience, and involves the precise regulation of the localization of synaptic proteins. However, the molecular mechanisms underlying activity-dependent organization of synaptic proteins remain unclear. We found that inhibition of the phosphorylation of the scaffold protein liprinα1 by neuronal activity promotes the synaptic localization of a major postsynaptic organizer, PSD-95, through increased liprinα1–PSD-95 interaction. This suggests that the phosphorylation status of liprinα1 functions as a molecular control for the activity-dependent localization of PSD-95 and hence postsynaptic organization and synapse maturation. Dysregulation of this post-translational process may lead to impaired synapse development. (See pp. E6992–E7001.)

Engineering the lutein epoxide cycle into *Arabidopsis thaliana*

Lauriebeth Leonelli, Matthew D. Brooks, and Krishna K. Niyogi

Optimizing the balance between light harvesting and photoprotection holds great promise for improving photosynthetic efficiency and ultimately crop yields. The switch between these two states is regulated by xanthophyll cycling, which occurs in response to changing light conditions. Two xanthophyll cycles have been described in vascular plants: the violaxanthin cycle and the lutein epoxide cycle. The contribution of the lutein epoxide cycle to photosynthesis has been difficult to dissect because the violaxanthin cycle often functions in parallel and responds more rapidly. The introduction of the lutein epoxide cycle into *Arabidopsis thaliana* creates a model system in which to study this ecologically significant but less well-characterized xanthophyll cycle and reveals its role in modulating a rapidly reversible component of nonphotochemical quenching of chlorophyll *a* fluorescence in response to light. (See pp. E7002–E7008.)

Dissecting and modeling zeaxanthin- and lutein-dependent nonphotochemical quenching in *Arabidopsis thaliana*

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The balance between light harvesting and photoprotection is a critical component of photosynthetic efficiency and must be maintained in fluctuating light conditions. Two xanthophylls play key roles in the vascular plant response to changes in light intensity: zeaxanthin and lutein. Chlorophyll fluorescence decay studies of *Arabidopsis thaliana* mutants enabling the isolation of individual contributions of zeaxanthin and lutein to the response and a kinetic model of quenching make it possible to model the mutant data and predict the combined influence of zeaxanthin

and lutein on nonphotochemical quenching in WT *A. thaliana* with the use of a single scaling factor. The model informs efforts to improve the response of plants to fluctuating light in natural environments and increase crop yields. (See pp. E7009–E7017.)

SPF45-related splicing factor for phytochrome signaling promotes photomorphogenesis by regulating pre-mRNA splicing in *Arabidopsis*

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Pre-mRNA processing not only enhances the diversity encoded in the genome without the need to increase the number of genes but also provides a means to adjust cellular transcript abundance. Environmental light has a profound effect on transcript accumulation, but how this is partitioned between transcriptional and posttranscriptional processes is largely unknown. Here we describe the identification and characterization of the splicing factor for phytochrome signaling (SFPS), which directly interacts with the photoreceptor phytochrome B. *sfps* seedlings are hyposensitive to light and display pre-mRNA splicing defects in a large number of genes, many of which regulate light signaling and the circadian clock. Thus, light might control pre-mRNA splicing in addition to transcription of many genes through SFPS to promote photomorphogenesis. (See pp. E7018–E7027.)