Lit Lunch 6-19-13

Fionn:

Nature Technology features

The challenge of big data

Nature biotechnology

Insect resistance to Bt crops: lessons from the first billion acres
Bruce E Tabashnik1, Thierry Brévault2 & Yves Carrière1

Evolution of resistance in pests can reduce the effectiveness of insecticidal proteins from *Bacillus thuringiensis* (Bt) produced by transgenic crops. We analyzed results of 77 studies from five continents reporting field monitoring data for resistance to Bt crops, empirical evaluation of factors affecting resistance or both. Although most pest populations remained susceptible, reduced efficacy of Bt crops caused by field-evolved resistance has been reported now for some populations of 5 of 13 major pest species examined, compared with resistant populations of only one pest species in 2005. Field outcomes support theoretical predictions that factors delaying resistance include recessive inheritance of resistance, low initial frequency of resistance alleles, abundant refuges of non-Bt host plants and two-toxin Bt crops deployed separately from one-toxin Bt crops. The results imply that proactive evaluation of the inheritance and initial frequency of resistance are useful for predicting the risk of resistance and improving strategies to sustain the effectiveness of Bt crops.

Ariel:

Structural systems biology evaluation of metabolic thermotolerance in Escherichia coli.

Chang RL, Andrews K, Kim D, Li Z, Godzik A, Palsson BO.

Source
Bioinformatics and Systems Biology Graduate Program, University of California San Diego, La Jolla, CA 92093-0412, USA.

Abstract
Genome-scale network reconstruction has enabled predictive modeling of metabolism for many systems. Traditionally, protein structural information has not been represented in such reconstructions. Expansion of a genome-scale model of Escherichia coli metabolism by including experimental and predicted protein structures enabled the analysis of protein thermostability in a network context. This analysis allowed the prediction of protein activities that limit network function at superoptimal temperatures and mechanistic interpretations of mutations found in strains adapted to heat. Predicted growth-limiting factors for thermotolerance were validated through nutrient supplementation experiments and defined metabolic sensitivities to heat stress, providing evidence that metabolic enzyme thermostability is rate-limiting at superoptimal temperatures. Inclusion of structural information expanded the content and predictive capability of genome-scale metabolic networks that enable structural systems biology of metabolism.

PMID: 23744946 [PubMed - indexed for MEDLINE]

Yichen:

Proc Natl Acad Sci U S A. 2013 Jun 11;110(24):9740-5. doi: 10.1073/pnas.1300221110. Epub 2013 May 29.

RNA polymerase approaches its promoter without long-range sliding along DNA.

Friedman LJ, Mumm JP, Gelles J.

Source

Department of Biochemistry, Brandeis University, Waltham, MA 02454.

Abstract

Sequence-specific DNA binding proteins must quickly bind target sequences, despite the enormously larger amount of nontarget DNA present in cells. RNA polymerases (or associated general transcription factors) are hypothesized to reach promoter sequences by facilitated diffusion (FD). In FD, a protein first binds to nontarget DNA and then reaches the target by a 1D sliding search. We tested whether Escherichia coli σ(54)RNA polymerase reaches a promoter by FD using the colocalization single-molecule spectroscopy (CoSMoS) multiwavelength fluorescence microscopy technique. Experiments directly compared the rates of initial polymerase binding to and dissociation from promoter and nonpromoter DNAs measured in the same sample under identical conditions. Binding to a nonpromoter DNA was much slower than binding to a promoter-containing DNA of the same length, indicating that the detected nonspecific binding events are not on the pathway to promoter binding. Truncating one of the DNA segments flanking the promoter to a length as short as 7 bp or lengthening it to ~3,000 bp did not alter the promoter-specific binding rate. These results exclude FD over distances corresponding to the length of the promoter or longer from playing any significant role in accelerating promoter search. Instead, the data support a direct binding mechanism, in which σ(54)RNA polymerase reaches the local vicinity of promoters by 3D diffusion through solution, and suggest that binding may be accelerated by atypical structural or dynamic features of promoter DNA. Direct binding explains how polymerase can quickly reach a promoter, despite occupancy of promoter-flanking DNA by bound proteins that would impede FD.

Proc Natl Acad Sci U S A. 2013 Jun 11;110(24):9986-91. doi: 10.1073/pnas.1305521110. Epub 2013 May 28.

Proteasome overload is a common stress factor in multiple forms of inherited retinal degeneration.

Lobanova ES, Finkelstein S, Skiba NP, Arshavsky VY.

Source

Albert Eye Research Institute, Duke University, Durham, NC 27710.

Abstract

Inherited retinal degenerations, caused by mutations in over 100 individual genes, affect approximately 2 million people worldwide. Many of the underlying mutations cause protein misfolding or mistargeting in affected photoreceptors. This places an increased burden on the protein folding and degradation machinery, which may trigger cell death. We analyzed how these cellular functions are affected in degenerating rods of the transducin γ-subunit (Gγ1) knockout mouse. These rods produce large amounts of transducin β-subunit (Gβ1), which cannot fold without Gγ1 and undergoes intracellular proteolysis instead of forming a transducin βγ-subunit complex. Our data revealed that the most critical pathobiological factor leading to photoreceptor cell death in these animals is insufficient capacity of proteasomes to process abnormally large amounts of misfolded protein. A decrease in the Gβ1 production in Gγ1 knockout rods resulted in a significant reduction in proteasomal overload and caused a striking reversal of photoreceptor degeneration. We further demonstrated that a similar proteasomal overload takes place in photoreceptors of other mutant mice where retinal degeneration has been ascribed to protein mistargeting or misfolding, but not in mice whose

photoreceptor degenerate as a result of abnormal phototransduction. These results establish the prominence of proteasomal insufficiency across multiple degenerative diseases of the retina, thereby positioning proteasomes as a promising therapeutic target for treating these debilitating conditions.

Keith:

Structural Dynamics of the MecA-ClpC Complex

A TYPE II AAA+ PROTEIN UNFOLDING MACHINE

June 14, 2013 The Journal of Biological Chemistry, 288, 17597-17608

Jing Liu, Ziqing Mei, Ningning Li, Yutao Qi, Yanji Xu, Yigong Shi, Feng Wang, Jianlin Lei and Ning Gao

School of Life Sciences, Tsinghua University, Beijing 100084, China

The MecA-ClpC complex is a bacterial type II AAA+ molecular machine responsible for regulated unfolding of substrates, such as transcription factors ComK and ComS, and targeting them to ClpP for degradation. The six subunits of the MecA-ClpC complex form a closed barrel-like structure, featured with three stacked rings and a hollow passage, where substrates are threaded and translocated through successive pores. Although the general concepts of how polypeptides are unfolded and translocated by internal pore loops of AAA+ proteins have long been conceived, the detailed mechanistic model remains elusive. With cryoelectron microscopy, we captured four different structures of the MecA-ClpC complexes. These complexes differ in the nucleotide binding states of the two AAA+ rings and therefore might presumably reflect distinctive, representative snapshots from a dynamic unfolding cycle of this hexameric complex. Structural analysis reveals that nucleotide binding and hydrolysis modulate the hexameric complex in a number of ways, including the opening of the N-terminal ring, the axial and radial positions of pore loops, the compactness of the C-terminal ring, as well as the relative rotation between the two nucleotide-binding domain rings. More importantly, our structural and biochemical data indicate there is an active allosteric communication between the two AAA+ rings and suggest that concerted actions of the two AAA+ rings are required for the efficiency of the substrate unfolding and translocation. These findings provide important mechanistic insights into the dynamic cycle of the MecA-ClpC unfoldase and especially lay a foundation toward the complete understanding of the structural dynamics of the general type II AAA+ hexamers.

A Self-compartmentalizing Hexamer Serine Protease from *Pyrococcus Horikoshii*

SUBSTRATE SELECTION ACHIEVED THROUGH MULTIMERIZATION

June 14, 2013 The Journal of Biological Chemistry, 288, 17884-17894.

Dóra K. Menyhárd, Anna Kiss-Szemán, Éva Tichy-Rács, Balázs Hornung, Krisztina Rádi, Zoltán Szeltner, Klarissza Domokos, Ilona Szamosi, Gábor Náray-Szabó, László Polgár and Veronika Harmat

Institute of Chemistry, Eötvös Loránd University, Pázmány Péter Sétány 1/A, H-1117 Budapest, Hungary

Oligopeptidases impose a size limitation on their substrates, the mechanism of which has long been under debate. Here we present the structure of a hexameric serine protease, an oligopeptidase from Pyrococcus horikoshii (PhAAP), revealing a complex, self-compartmentalized inner space, where substrates may access the monomer active sites passing through a double-gated “check-in” system, first passing through a pore on the hexamer surface and then turning to enter through an even smaller opening at the monomers' domain

interface. This substrate screening strategy is unique within the family. We found that among oligopeptidases, a residue of the catalytic apparatus is positioned near an amylogenic β-edge, which needs to be protected to prevent aggregation, and we found that different oligopeptidases use different strategies to achieve such an end. We propose that self-assembly within the family results in characteristically different substrate selection mechanisms coupled to different multimerization states.

Indu:

1. Science. 2013 May 24;340(6135):978-81. doi: 10.1126/science.1234055.

Futile protein folding cycles in the ER are terminated by the unfolded protein O-mannosylation pathway.

Xu C, Wang S, Thibault G, Ng DT.

Temasek Life Sciences Laboratory, National University of Singapore, Singapore.

Comment in Science. 2013 May 24;340(6135):930-1.

Newly synthesized polypeptides fold and assemble with assistance from protein chaperones. Full maturation can take multiple attempts, exchanging chaperones at each round. Improperly folded molecules must exit folding cycles and be degraded. In the endoplasmic reticulum (ER), prolonged substrate cycling is detrimental because it expends chaperone and energy resources and increases toxic reactive oxygen species. In budding yeast, we found that unfolded protein O-mannosylation terminated failed folding attempts through the Pmt1/Pmt2 complex. O-mannosylation incapacitated target molecule folding and removed them from folding cycles by reducing engagement with the Kar2 chaperone. In an in vitro protein refolding assay, the modification intrinsically and irreversibly disabled the folding potential of the substrate. Thus, protein folding termination can involve a covalent glycosylation event.

PMID: 23704572 [PubMed - indexed for MEDLINE]

2. Science. 2013 May 24;340(6135):984-7. doi: 10.1126/science.1235264. Epub 2013 May 9.

The human malaria parasite Pfs47 gene mediates evasion of the mosquito immune system.

Molina-Cruz A, Garver LS, Alabaster A, Bangiolo L, Haile A, Winikor J, Ortega C, van Schaijk BC, Sauerwein RW, Taylor-Salmon E, Barillas-Mury C.

Laboratory of Malaria and Vector Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rockville, MD 20892, USA.

Comment in Science. 2013 May 24;340(6135):936-7.

Plasmodium falciparum transmission by Anopheles gambiae mosquitoes is remarkably efficient, resulting in a very high prevalence of human malaria infection in sub-Saharan Africa. A combination of genetic mapping, linkage group selection, and functional genomics was used to identify Pfs47 as a P. falciparum gene that allows the parasite to infect A. gambiae without activating the mosquito immune system. Disruption of Pfs47 greatly reduced parasite survival in the mosquito, and this phenotype could be reverted by genetic complementation of the parasite or by disruption of the mosquito complement-like system. Pfs47 suppresses midgut nitration responses that are critical to activate the complement-like system. We provide direct experimental evidence that immune evasion mediated by Pfs47 is critical for efficient human malaria transmission by A. gambiae.

PMID: 23661646 [PubMed - indexed for MEDLINE]

3. Science. 2013 May 24;340(6135):976-8. doi: 10.1126/science.1234864. Epub 2013 Apr 11.

Ribosomal protein SA haploinsufficiency in humans with isolated congenital asplenia.

Bolze A, Mahlaoui N, Byun M, Turner B, Trede N, Ellis SR, Abhyankar A, Itan Y, Patin E, Brebner S, Sackstein P, Puel A, Picard C, Abel L, Quintana-Murci L, Faust SN, Williams AP, Baretto R, Duddridge M, Kini U, Pollard AJ, Gaud C, Frange P, Orbach D, Emile JF, Stephan JL, Sorensen R, Plebani A, Hammarstrom L, Conley ME, Selleri L, Casanova JL.

St. Giles Laboratory of Human Genetics of Infectious Diseases, Rockefeller University, New York, NY 10065, USA.

Isolated congenital asplenia (ICA) is characterized by the absence of a spleen at birth in individuals with no other developmental defects. The patients are prone to life-threatening bacterial infections. The unbiased analysis of exomes revealed heterozygous mutations in RPSA in 18 patients from eight kindreds, corresponding to more than half the patients and over one-third of the kindreds studied. The clinical penetrance in these kindreds is complete. Expression studies indicated that the mutations carried by the patients-a nonsense mutation, a frameshift duplication, and five different missense mutations-cause autosomal dominant ICA by haploinsufficiency. RPSA encodes ribosomal protein SA, a component of the small subunit of the ribosome. This discovery establishes an essential role for RPSA in human spleen development.

PMCID: PMC3677541
PMID: 23579497 [PubMed - indexed for MEDLINE]

Stephanie:

From TIBS:

Opinion: Folding the Proteome

Ether Braselmann, Julie L. Chaney, and Patricia Clark
Department Chemistry and Biochemistry, University of Notre Dame

Protein folding is an essential prerequisite for protein function and hence cell function. Kinetic and thermodynamic studies of small proteins that refold reversibly were essential for developing our current understanding of the fundamentals of protein folding mechanisms. However, we still lack sufficient understanding to accurately predict protein structures from sequences, or the effects of disease-causing mutations. To date, model proteins selected for folding studies represent only a small fraction of the complexity of the proteome and are unlikely to exhibit the breadth of folding mechanisms used in vivo. We are in urgent need of new methods – both theoretical and experimental – that can quantify the folding behavior of a truly broad set of proteins under in vivo conditions. Such a shift in focus will provide a more comprehensive framework from which to understand the connections between protein folding, the molecular basis of disease, and cell function and evolution.

From Plant Mol Biol

Original Article: BAC-end sequences analysis provides first insights into coffee (Coffea canephora P.) genome composition and evolution

Alexis Dereeper • Romain Guyot • Christine Tranchant-Dubreuil • Franc¸ois Anthony • Xavier Argout • Fabien de Bellis • Marie-Christine Combes • Frederick Gavory • Alexandre de Kochko • Dave Kudrna • Thierry Leroy • Julie Poulain • Myriam Rondeau • Xiang Song • Rod Wing • Philippe Lashermes

Abstract: Coffee is one of the world's most important agricultural commodities. Coffee belongs to the Rubiaceae family in the euasterid I clade of dicotyledonous plants, to which the Solanaceae family also belongs. Two bacterial artificial chromosome (BAC) libraries of a homozygous doubled haploid plant of Coffea canephora were constructed using two enzymes, HindIII and BstYI. A total of 134,827 high quality BAC-end sequences (BESs) were generated from the 73,728 clones of the two libraries, and 131,412 BESs were conserved for further analysis after elimination of chloroplast and mitochondrial sequences. This corresponded to almost 13 % of the estimated size of the C. canephora genome. 6.7 % of BESs contained simple sequence repeats, the most abundant (47.8 %) being mononucleotide motifs. These sequences allow the development of numerous useful marker sites. Potential transposable elements (TEs) represented 11.9 % of the full length BESs. A difference was observed between the BstYI

and HindIII libraries (14.9 vs. 8.8 %). Analysis of BESs against known coding sequences of TEs indicated that 11.9 % of the genome corresponded to known repeat sequences, like for other flowering plants. The number of genes in the coffee genome was estimated at 41,973 which is probably overestimated. Comparative genome mapping revealed that microsynteny was higher between coffee and grapevine than between coffee and tomato or Arabidopsis. BESs constitute valuable resources for the first genome wide survey of coffee and provide new insights into the composition and evolution of the coffee genome.

Damian:

Van oosten-Hawle, P., Porter, Robert s., and Morimoto, Richard i. (2013). Regulation of Organismal Proteostasis by Transcellular Chaperone Signaling. Cell 153, 1366-1378.

A major challenge for metazoans is to ensure that different tissues, each expressing distinctive proteomes, are nevertheless well protected at an organismal level from proteotoxic stress. We show that expression of endogenous metastable proteins in muscle cells, which rely on chaperones for proper folding, induces a systemic stress response throughout multiple tissues of C. elegans. Suppression of misfolding in muscle cells can be achieved not only by enhanced expression of HSP90 in muscle cells but as effectively by elevated expression of HSP90 in intestine or neuronal cells. This cell-nonautonomous control of HSP90 expression relies upon transcriptional feedback between somatic tissues that is regulated by the FoxA transcription factor PHA-4. This transcellular chaperone signaling response maintains organismal proteostasis when challenged by a local tissue imbalance in folding and provides the basis for organismal stress-sensing surveillance.

Liyuan:

Responses ofNannochloropsis oceanicaIMET1 to Long-Term Nitrogen Starvation and Recovery

Hong-Po Dong, Ernest Williams, Da-zhi Wang, Zhang-Xian Xie, Ru-ching Hsia, Alizée Jenck, Rolf Halden, Jing Li, Feng Chen, and Allen R. Place*

The Nannochloropsis genus contains oleaginous microalgae that have served as model systems for developing renewable biodiesel. Recent genomic and transcriptomic studies onNannochloropsisspecies have provided insights into the regulation of lipid production in response to nitrogen stress. Previous studies have focused on the responses of Nannochloropsisspecies to short-term nitrogen stress, but the effect of long-term nitrogen deprivation remains largely unknown. In this study, physiological and proteomic approaches were combined to understand the mechanisms by whichNannochloropsis oceanicaIMET1 is able to endure long-term nitrate deprivation and its ability to recover homeostasis when nitrogen is amended. Changes of the proteome during chronic nitrogen starvation espoused the physiological changes observed, and there was a general trend toward recycling
nitrogen and storage of lipids. This was evidenced by a global down-regulation of protein expression, a retained expression of proteins involved in glycolysis and the synthesis of fatty acids, as well as an up-regulation of enzymes used in nitrogen scavenging and protein turnover. Also, lipid accumulation and autophagy of plastids may play a key role in maintaining cell vitality. Following the addition of nitrogen, there were proteomic changes and metabolic changes observed within 24 h, which resulted

in a return of the culture to steady state within 4 d. These results demonstrate the ability ofN. oceanicaIMET1 to recover from long periods of nitrate deprivation without apparent detriment to the culture and provide proteomic markers for genetic modification.

Gene regulation by the act of long non-coding RNA transcription
Aleksandra E Kornienko, Philipp M Guenzl, Denise P Barlow and Florian M Pauler

Abstract
Long non-protein-coding RNAs (lncRNAs) are proposed to be the largest transcript class in the mouse and human transcriptomes. Two important questions are whether all lncRNAs are functional and how they could exert a function. Several lncRNAs have been shown to function through their product, but this is not the only possible mode of action. In this review we focus on a role for the process of lncRNA transcription, independent of the lncRNA product, in regulating protein-coding-gene activityin
cis. We discuss examples where lncRNA transcription leads to gene silencing or activation, and describe strategies to determine if the lncRNA product or its transcription causes the regulatory effect.

Elizabeth:

Chang RL, Andrews K, Kim D, Li Z, Godzik A, Palsson BO.
Structural systems biology evaluation of metabolic thermotolerance in Escherichia coli.
Science. 2013 Jun 7;340(6137):1220-3.
PMID: 23744946 [PubMed - in process]

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Hsp110 is a bona fide chaperone using ATP to unfold stable misfolded polypeptides and reciprocally collaborate with Hsp70 to solubilize protein aggregates.
J Biol Chem. 2013 Jun 4;. [Epub ahead of print]
PMID: 23737532 [PubMed - as supplied by publisher]

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PMID: 23736536 [PubMed - as supplied by publisher]

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PMID: 23741796 [PubMed - in process]

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The role of eEF2 pathway in learning and synaptic plasticity.
Neurobiol Learn Mem. 2013 Jun 3;. [Epub ahead of print]
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A Rapid Ribosome Profiling Method Elucidates Chloroplast Ribosome Behavior in Vivo.
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PMID: 23735295 [PubMed - as supplied by publisher]

Oxidative Folding in Chloroplasts

Thomas Kieselbach

Antioxidants & Redox Signaling, Vol. 19, No. 1, July 2013: 72-82.

Disulfide Bond Formation in the Cytoplasm

Mirva J. Saaranen and Lloyd W. Ruddock

Antioxidants & Redox Signaling, Vol. 19, No. 1, July 2013: 36-43.

FEBs Journal
The ORF *slr0091* of *Synechocystis* sp. PCC6803 Encodes a High-light Induced Aldehyde Dehydrogenase Converting Apocarotenals and Alkanals
Danika Trautmann, Peter Beyer and Salim Al-Babili
Accepted manuscript online: 5 JUN 2013 02:17AM EST | DOI: 10.1111/febs.12361

Auxin-mediated nitrate signalling by NRT1.1 participates in the adaptive response of ***Arabidopsis*** root architecture to the spatial heterogeneity of nitrate availability
EMMANUELLE MOUNIER, MARJORIE PERVENT, KARIN LJUNG, ALAIN GOJON and PHILIPPE NACRY
Accepted manuscript online: 3 JUN 2013 09:02PM EST | DOI: 10.1111/pce.12143

Plant, Cell & Environment Content Alert (New Articles)
The impact of environmental stress on male reproductive development in plants – biological processes and molecular mechanisms
NICO de STORME and DANNY GEELEN
Accepted manuscript online: 3 JUN 2013 08:58PM EST | DOI: 10.1111/pce.12142

How do trees die? A test of the hydraulic failure and carbon starvation hypotheses
SANNA SEVANTO, NATE G. MCDOWELL, L. TURIN DICKMAN, ROBERT PANGLE and WILLIAM T. POCKMAN
Accepted manuscript online: 3 JUN 2013 08:58PM EST | DOI: 10.1111/pce.12141

Invited Reviews

Modeling Stomatal Conductance in Response to Environmental Factors
THOMAS N. BUCKLEY and KEITH A. MOTT
Accepted manuscript online: 3 JUN 2013 08:58PM EST | DOI: 10.1111/pce.12140

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Nat Struct Mol Biol. 2013 Apr;20(4):409-10.
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Hemoglobin regulation of plant embryogenesis and plant pathogen interaction.
Plant Signal Behav. 2013 Jun 7;8(8). [Epub ahead of print]
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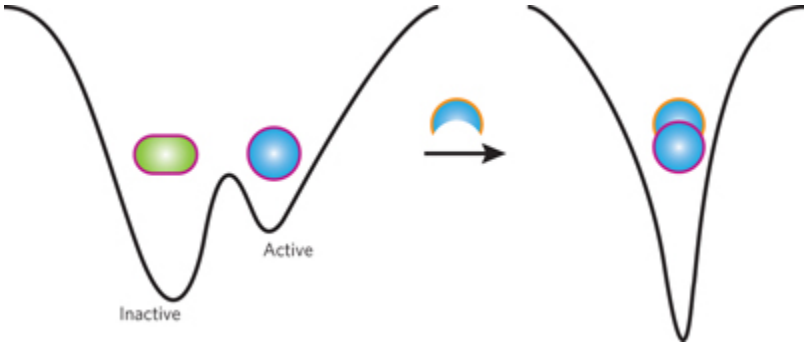
Linking genes of unknown function with abiotic stress responses by high-throughput phenotype screening.
Luhua S, Hegie A, Suzuki N, Shulaev E, Luo X, Cenariu D, Ma V, Kao S, Lim J, Gunay MB, Oosumi T, Lee SC, Harper J, Cushman J, Gollery M, Girke T, Bailey-Serres J, Stevenson RA, Zhu JK, Mittler R.

Nature Chemical Biology Contents: July 2013 Volume 9 Number 7, pp 408 - 466

Protein dynamics: Catch them if you can
Gianluigi Veglia Nature Chemical Biology 9, 466 (2013)

Allosteric inhibition through suppression of transient conformational states pp462 - 465
Shiou-Ru Tzeng and Charalampos G Kalodimos
doi:10.1038/nchembio.1250



Advanced NMR studies of catabolite activator protein show that allosteric inhibitors can prevent conformational changes needed for a protein to bind its ligand, offering an explanation for why these inhibitors may not appear to cause any effect when monitored using static techniques.

Biosensors for phytohormone quantification: challenges, solutions, and opportunities
Review Article
Pages 244-249
Darren M. Wells, Laurent Laplaze, Malcolm J. Bennett, Teva Vernoux

Trends In Plant Science

RNA-Seq: revelation of the messengers

Pages 175-179
Marcel C. Van Verk, Richard Hickman, Corné M.J. Pieterse, Saskia C.M. Van Wees

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Highlights

► RNA-Seq offers a dynamic range of mRNA quantification at low technical variability ► Choice of the right protocols, tools, and methods are critical for RNA-Seq success ► Multireads can drastically affect the outcome of RNA-Seq experiments ► Appropriate normalization is critical prior to testing for differential expression