

Molecular BioSystems

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IN THIS ISSUE

ISSN 1742-206X CODEN MBOIBW 4(6) 445-696 (2008)



Cover

See E. Esquenazi *et al.*, pp. 562–570.
An epifluorescent (ex 590 nm) image of the marine sponge *Dysidea herbacea* overlaid with MALDI-TOF MS results showing the presence and localization of two different metabolite ions, depicted in blue and green. Image reproduced by permission of Eduardo Esquenazi, Cameron Coates, Luke Simmons, David Gonzalez, William H. Gerwick and Pieter C. Dorrestein from *Molecular BioSystems*, 2008, **4**, 562.



Inside cover

See P. S. Marinec *et al.*, pp. 571–578.
Bifunctional Q1 molecules evade cytochrome P450 metabolism by forming protective complexes with FK506-binding protein. Image reproduced by permission of Paul S. Marinec, Jody K. Lancia and Jason E. Gestwicki from *Molecular BioSystems*, 2008, **4**, 571.

CHEMICAL BIOLOGY

B41

Drawing together the research highlights and news from all RSC publications, *Chemical Biology* provides a 'snapshot' of the latest developments in chemical biology, showcasing newsworthy articles and significant scientific advances.

Chemical Biology

June 2008/Volume 3/Issue 6

www.rsc.org/chembiology

EDITORIAL

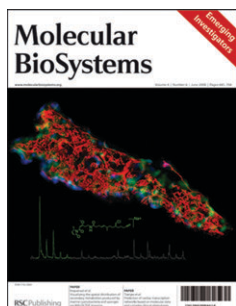
465

Emerging Investigators issue

The chair of the *Molecular BioSystems* Editorial Board, Professor Tom Kodadek, introduces the Emerging Investigators issue.



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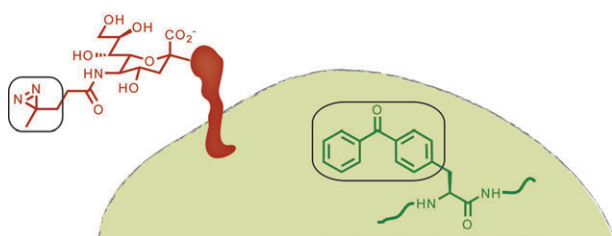


Contributors to the Emerging Investigators issue

Molecular BioSystems profiles the contributors to the Emerging Investigators issue.

REVIEW ARTICLES

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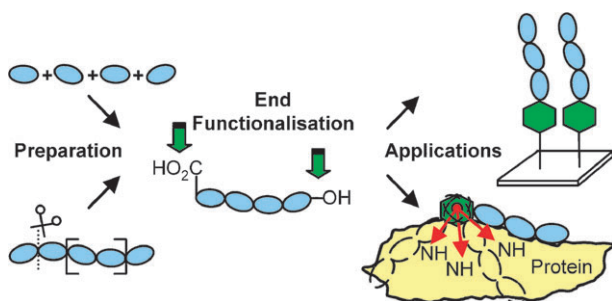


Photocrosslinkers illuminate interactions in living cells

Yoshihito Tanaka, Michelle R. Bond and Jennifer J. Kohler*

This review highlights recent methodological developments that make it possible to introduce photocrosslinking groups into polypeptides or glycans as they are synthesized in cells and how these methods offer a non-invasive way to study macromolecular interactions in a native context.

481



Enabling methodology for the end functionalisation of glycosaminoglycan oligosaccharides

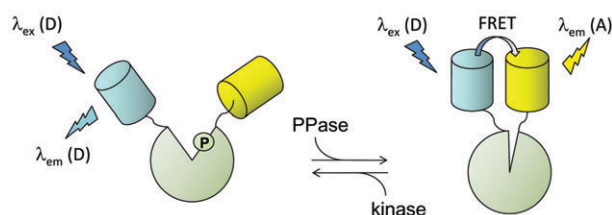
Emiliano Gemma, Odile Meyer, Dušan Uhrin and Alison N. Hulme*

We review methods for the preparation of end-functionalised glycosaminoglycan (GAG) oligosaccharides which may be used for a wide range of applications, including the study of GAG–protein complexes and the synthesis of GAG arrays.

COMMUNICATIONS



496



Visualization of phosphatase activity in living cells with a FRET-based calcineurin activity sensor

Robert H. Newman and Jin Zhang*

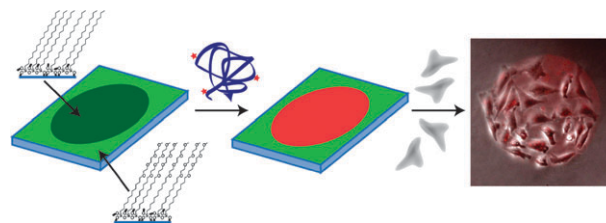
We describe the first genetically-encodable phosphatase activity biosensor designed to specifically track calcineurin activity inside living cells. The successful design of a prototype phosphatase activity sensor lays a foundation for studying targeting and compartmentation of phosphatases.

502

Direct printing of trichlorosilanes on glass for selective protein adsorption and cell growth

Dawn M. Yanker and Joshua A. Maurer*

Direct patterning of octadecyltrichlorosilane and backfilling with a glycol-terminated trichlorosilane on glass creates a surface on which protein adsorption and cell growth can be manipulated.

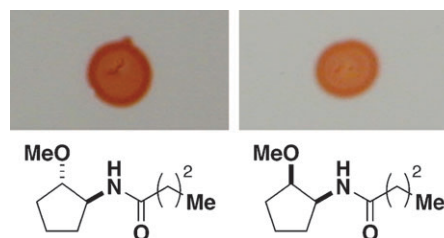


505

2-Methoxycyclopentyl analogues of a *Pseudomonas aeruginosa* quorum sensing modulator

Lydia Y. W. Lee, Timothy Hupfield, Rebecca L. Nicholson, James T. Hodgkinson, Xianbin Su, Gemma L. Thomas, George P. C. Salmond, Martin Welch and David R. Spring*

Cis- and *trans*-2-methoxycyclopentyl analogues of a quorum sensing molecule were synthesized and screened in *P. aeruginosa* and *Serratia* 39006 phenotypic assays. Both were agonists, but less active relative to a 2-oxocyclopentyl analogue and the cognate ligand.

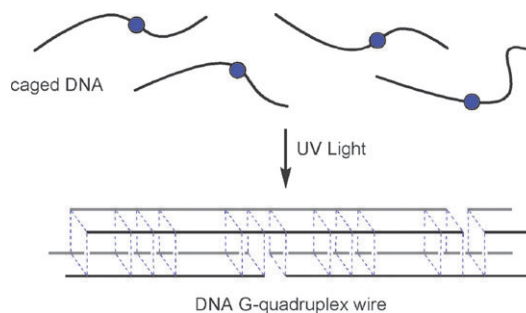


508

Light-activated deoxyguanosine: photochemical regulation of peroxidase activity

Hrvoje Lusic, Mark O. Lively and Alexander Deiters*

A novel photocaged deoxyguanosine phosphoramidite was synthesized and incorporated into DNA. Peroxidase deoxyribozymes carrying the caged dG were catalytically inactive due to inhibition of structural organization. Brief UV irradiation efficiently restored the formation of a G-quadruplex wire and peroxidase activity.

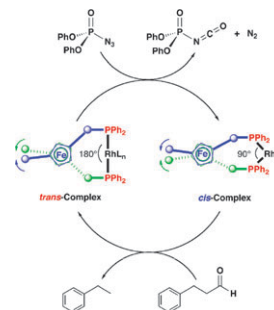


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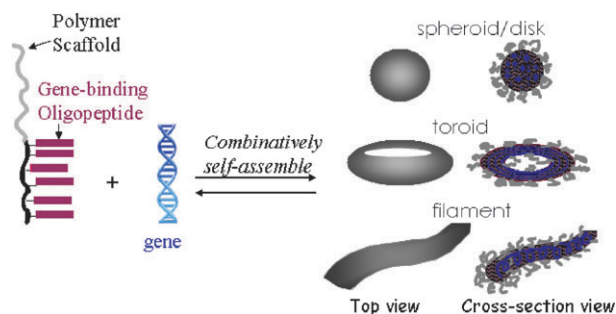
Toward autonomously operating molecular machines driven by transition-metal catalyst

Kenichi Tanaka and Kazushi Kinbara*

A Vaska-type complex carrying a ferrocene-appended diphosphine ligand was developed as a prototype of autonomous molecular machines that is able to undergo continuous scissoring motion in the presence of diphenylphosphoryl azide and aldehyde.



515

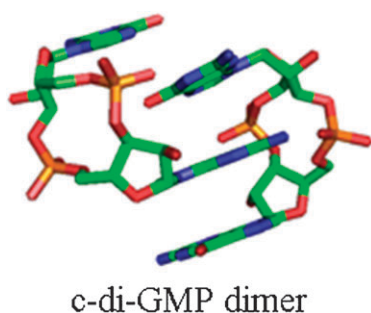


DNA packaging *via* combinative self-assembly

Jennifer Haley, Xiaolin Li, Nicholas Marshall, Jason Locklin and Yan Geng*

A novel and versatile DNA packaging approach was developed by grafting DNA-binding oligopeptides onto a polymer scaffold to combinatively self-assemble with DNA into compact nanostructures.

518



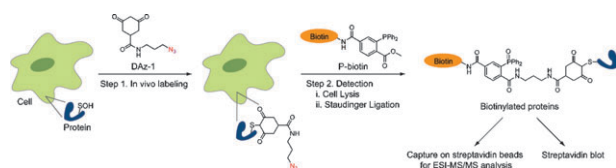
A simple solid-phase synthesis of the ubiquitous bacterial signaling molecule, c-di-GMP and analogues

Irene Kiburu, Andrew Shurer, Lei Yan and Herman O. Sintim*

Cyclic-di-guanylate (c-di-GMP) has emerged as a general and important signaling molecule uniquely present in bacteria. We herein provide a simple solid-phase synthesis of c-di-GMP using an automated DNA synthesizer for the majority of the synthesis.

PAPERS

521

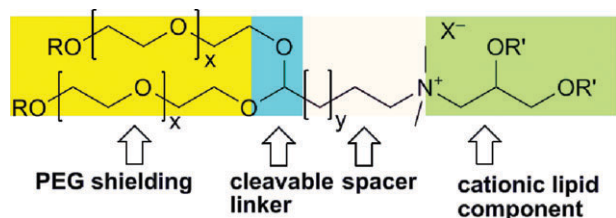


A chemical approach for detecting sulfenic acid-modified proteins in living cells

Khalilah G. Reddie, Young Ho Seo, Wilson B. Muse III, Stephen E. Leonard and Kate S. Carroll*

We have developed a method that enables live cell labeling of sulfenic acid-modified proteins. This method employs a new probe DAZ-1 that is chemoselective for sulfenic acids, cell permeable and contains an azide chemical handle that can be selectively detected with bio-orthogonal phosphine reagents for identification and visualization.

532



Acid cleavable PEG-lipids for applications in a ternary gene delivery vector

John B. Wong, Stephanie Grosse, Alethea B. Tabor, Stephen L. Hart and Helen C. Hailes*

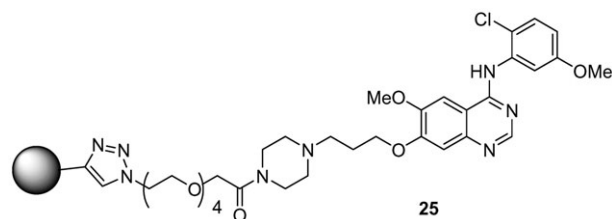
A novel class of pH-sensitive PEG lipids bearing acid-cleavable acetal linkages and short PEG chains have been synthesised and used in ternary vector formulations. The cleavage pH was influenced by structural components including the terminal PEG moiety and spacer length.

542

Design, synthesis and characterization of “clickable” 4-anilinoquinazoline kinase inhibitors

B. Gayani K. Perera and Dustin J. Maly*

A versatile method for the generation of “clickable” 4-anilinoquinazoline kinase inhibitors is reported. This methodology was used to generate potent and selective inhibitors of Aurora A, p38 and Src that can be modified *via* the Huisgen 1,3-dipolar cycloaddition.

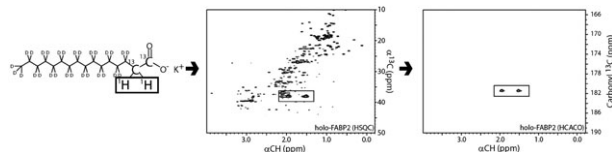


551

Design, synthesis, and evaluation of an isotopic labeling strategy for studying fatty acid–protein binding by NMR

Yong Han, Timothy E. Alexander and Gregory P. Tochtrop*

We illustrate the utility of a fatty acid isotopic labeling strategy to study protein ligand binding using FABP2 as proof of principle.

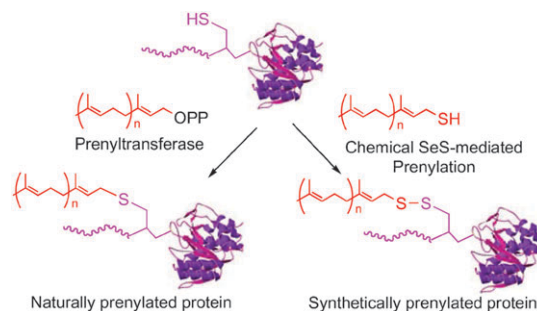


558

Chemical site-selective prenylation of proteins

David P. Gamblin, Sander van Kasteren, Gonçalo J. L. Bernardes, Justin M. Chalker, Neil J. Oldham, Antony J. Fairbanks and Benjamin G. Davis*

A direct thionation procedure allows conversion of allylic alcohols into the corresponding thiols, the products of which are immediately compatible with one-pot site-selective selenenyl sulfide mediated protein conjugation.

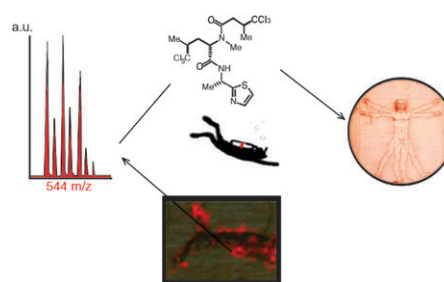


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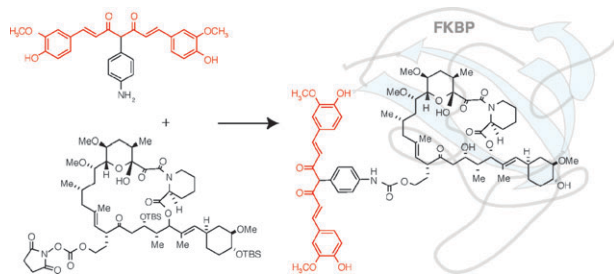
Visualizing the spatial distribution of secondary metabolites produced by marine cyanobacteria and sponges *via* MALDI-TOF imaging

Eduardo Esquenazi, Cameron Coates, Luke Simmons, David Gonzalez, William H. Gerwick and Pieter C. Dorrestein*

MALDI-TOF imaging is a promising tool in marine natural products research: it gives us the ability to visualize the presence and distribution of bioactive compounds in both simple and complex assemblages of intact marine organisms.



571

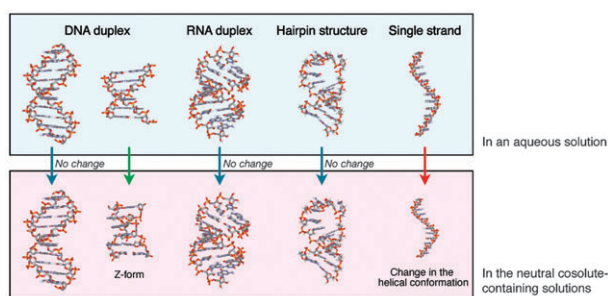


Bifunctional molecules evade cytochrome P₄₅₀ metabolism by forming protective complexes with FK506-binding protein

Paul S. Marinec, Jody K. Lancia and Jason E. Gestwicki*

FK506 has a surprisingly good pharmacology, despite its high molecular weight. We modified unrelated compounds, such that they also acquire affinity for FKBP. Strikingly, these derivatives become resistant to metabolism *in vitro*. These findings suggest one mechanism that is responsible for FK506's long half-life *in vivo*.

579

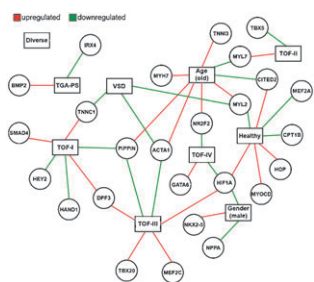


Conformation and the sodium ion condensation on DNA and RNA structures in the presence of a neutral cosolute as a mimic of the intracellular media

Shu-ichi Nakano,* Lei Wu, Hirohito Oka, Hisae Tateishi Karimata, Toshimasa Kirihaata, Yuichi Sato, Satoshi Fujii, Hiroshi Sakai, Masayuki Kuwahara, Hiroaki Sawai and Naoki Sugimoto*

Comprehensive studies of the conformations and the thermal stabilities of DNA and RNA structures in cosolute-containing solutions implicated the significance of the intracellular environment on nucleotide structures in a cell.

589

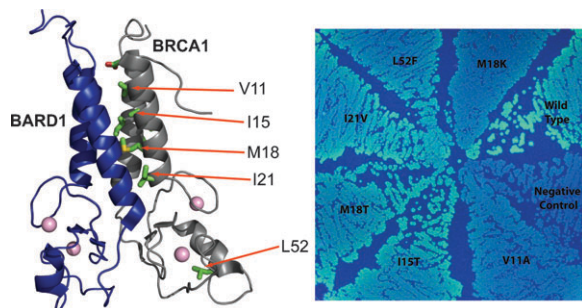


Prediction of cardiac transcription networks based on molecular data and complex clinical phenotypes

Martje Toenjes, Markus Schueler, Stefanie Hammer, Utz J. Pape, Jenny J. Fischer, Felix Berger, Martin Vingron and Silke Sperling*

An integrative approach to identifying cardiac transcription networks based on correlated gene expression and optimized prediction of transcription factor binding sites can enable explanation of gene expression profiles observed for congenital heart disease.

599



Re-engineering a split-GFP reassembly screen to examine RING-domain interactions between BARD1 and BRCA1 mutants observed in cancer patients

Mohosin Sarkar and Thomas J. Magliery*

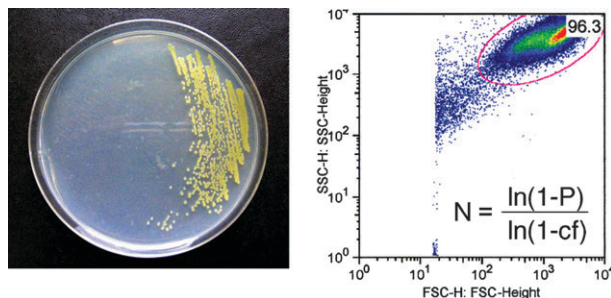
We re-engineered the split-GFP system for fast reassembly and bright fluorescence with whole protein domains. The improved system was used to study interactions of BARD1 with cancer-associated mutants of the tumor suppressor BRCA1.

606

Estimating P-coverage of biosynthetic pathways in DNA libraries and screening by genetic selection: biotin biosynthesis in the marine microorganism *chromohalobacter*

Eun Jin Kim, Scott Angell, Jeff Janes and Coran M. H. Watanabe*

An algorithm called BPC is put forth to estimate the size of a library necessary to achieve proper coverage of biosynthetic pathways housed within microbial genomes. Genetic selection is demonstrated as a method to identify and localize biosynthetic gene clusters within metagenomic DNA libraries.

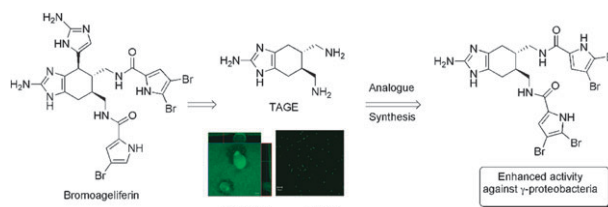


614

Control of bacterial biofilms with marine alkaloid derivatives

Robert W. Huigens III, Luyan Ma, Christopher Gambino, Peter D. R. Moeller, Anne Basso, John Cavanagh, Daniel J. Wozniak and Christian Melander*

Bacterial biofilms are responsible for a plethora of medical problems. Herein we report the identification of bicyclic 2-aminoimidazole derivatives that inhibit and disperse bacterial biofilms.



622

Characterization of TioF, a tryptophan 2,3-dioxygenase involved in 3-hydroxyquinaldic acid formation during thiocoraline biosynthesis

Anita Sheoran, Andrew King, Ana Velasco, Jessica M. Pero and Sylvie Garneau-Tsodikova*

TioF, a new member of the family of tryptophan 2,3-dioxygenases with broader substrate specificity than other TDOs, is involved in the formation of the marine anticancer agent thiocoraline.

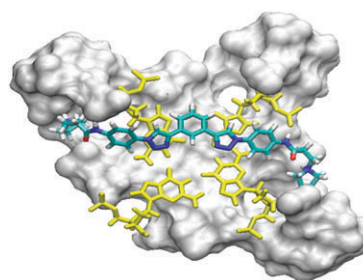


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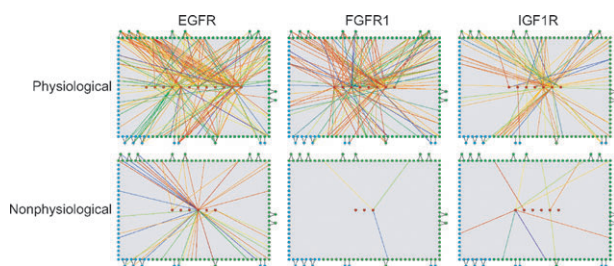
Targeting telomerase and telomeres: a click chemistry approach towards highly selective G-quadruplex ligands

Adam D. Moorhouse, Shozeb Haider, Mekala Gunaratnam, Deeksha Munnur, Stephen Neidle* and John E. Moses*

A library of new telomerase inhibitors have been discovered utilizing the Cu(I) catalyzed 'Click' reaction between a azides and terminal alkynes. These 'click' ligands show promising activity and selectivity *in vivo* against telomerase.



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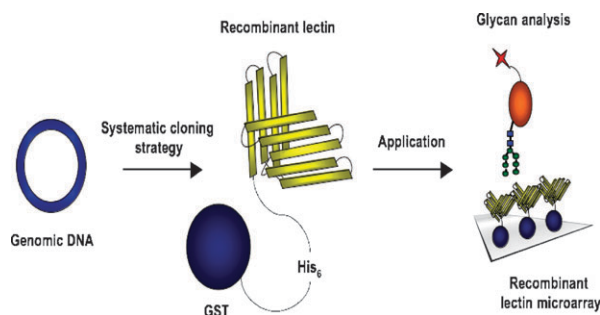


A quantitative study of the recruitment potential of all intracellular tyrosine residues on EGFR, FGFR1 and IGF1R

Alexis Kaushansky, Andrew Gordus, Bryan Chang, John Rush and Gavin MacBeath*

This paper reports quantitative interaction maps for EGFR, FGFR1 and IGF1R, obtained by probing protein microarrays comprising human SH2 and PTB domains with phosphopeptides representing every intracellular tyrosine residue on each of the three receptors.

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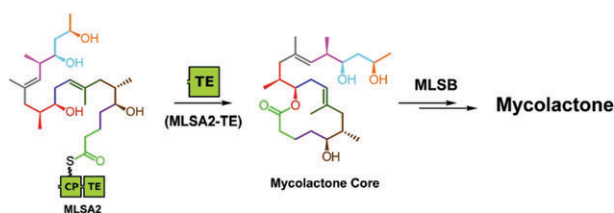


A simple strategy for the creation of a recombinant lectin microarray

Ku-Lung Hsu, Jeffrey C. Gildersleeve and Lara K. Mahal*

We describe an efficient strategy for the systematic creation of bacterially-derived recombinant lectins for use in lectin microarray technology. We demonstrate that a recombinant lectin microarray is capable of distinguishing glycopatterns of protein and tumor cell samples.

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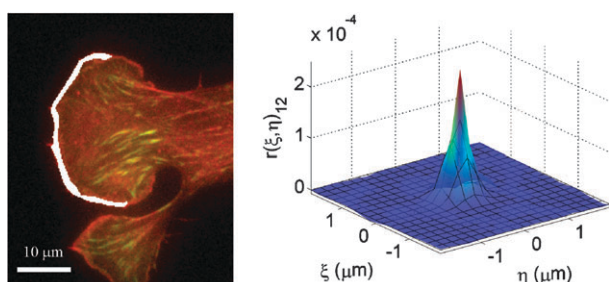


The unusual macrocycle forming thioesterase of mycolactone

Jordan L. Meier, Tiffany Barrows-Yano, Timothy L. Foley, Candice L. Wike and Michael D. Burkart*

The putative macrocycle forming thioesterase MLSA2 TE was cloned, expressed and biochemically characterized. The findings suggest that the enzyme utilizes a unique biochemical mechanism for macrocycle formation.

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Accurate measurements of protein interactions in cells via improved spatial image cross-correlation spectroscopy

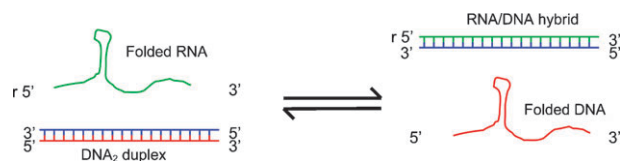
Jonathan W. D. Comeau, David L. Kolin and Paul W. Wiseman*

New strategies to overcome some of the limitations of spatial image cross-correlation spectroscopy promise to significantly improve the dynamic range and practical usage of an accurate method for measuring molecular interactions *via* analysis of fluorescence microscopy images.

Thermodynamic prediction of RNA–DNA duplex-forming regions in the human genome

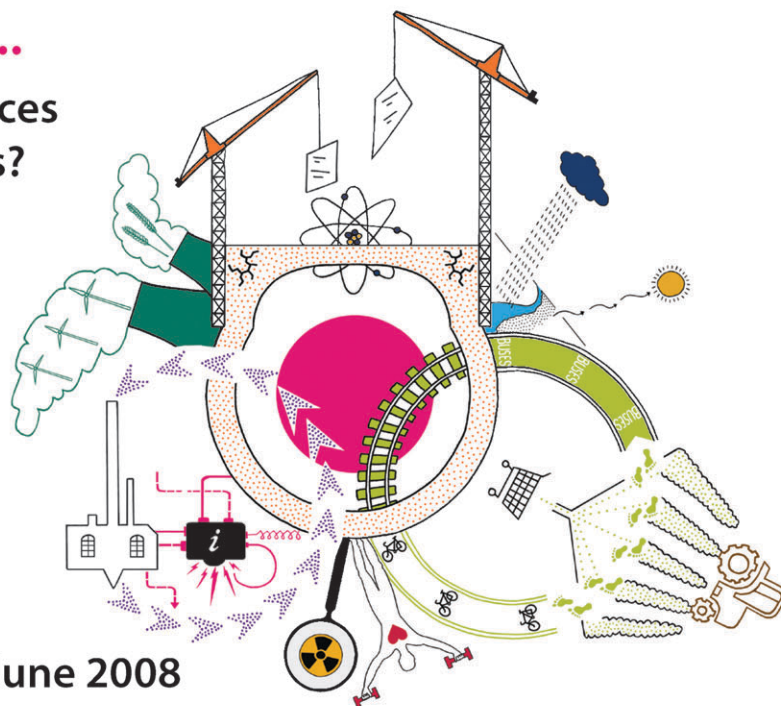
Julian L. Huppert*

The energetic contributions of both duplex formation and single-strand folding are considered and used to search the entire human genome for regions predicted to form RNA–DNA hybrids, confirming previous experiments.



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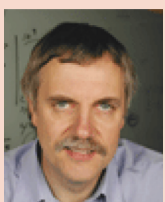
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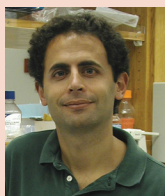
"Chemists will increasingly turn to '-omics' approaches to understand mechanism of action and specificity of bioactive molecules. Molecular BioSystems provides a home for this rapidly developing interdisciplinary science."

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Chair, Editorial Board



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Ruedi Aebersold,
Former Editorial Board member



"Congratulations on the excellent start – I am sure this [impact factor] number will continue to rise over the coming years."

Benjamin Cravatt,
Editorial Board member



"We received three excellent, tractable, and critical reviews with a rapid turn around time after submitting our manuscript. In today's world of potentially long times from submission to publication, this was very refreshing."

Mike Washburn
Advisory Board Member



"We believe Molecular BioSystems has more to offer the chemical biology community than any other journal."

Michael Smith,
Commissioning Editor

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