EDITORIAL
385 Five years of Nature Chemical Biology

SPECIAL FEATURE
387 Five years in review

COMMENTARY
390 Biosynthesis: Is it time to go retro?
Brian O Bachmann

RESEARCH HIGHLIGHTS
394 Our choices from the recent literature

NEWS AND VIEWS
397 High-content screens: Giving Rho(d) directions
Markus K Muellner & Sebastian M B Nijman
► Article p457

398 Synthetic biology: Designer bacteria degrades toxin
John R Kirby
► Article p464

400 Cell biology: Manipulating proteostasis
Richard N Sifers
► Article p424

401 Lipids: COX-2’s new role in inflammation
Chu Chen
► Article p433

403 Polymerases: Glycan chain-length control
Chris Whitfield
► Article p418

ON THE COVER
Screening
A new Rhod map
Article p457; News & Views p397

Protein folding
Gaucher’s shapeshifter
Article p424; News & Views p400

Metabolism
Pluripotent potentials
Article p411
BRIEF COMMUNICATIONS

405  A direct NMR method for the measurement of competitive kinetic isotope effects
J Chan, A R Lewis, M Gilbert, M-F Karwaski & A J Bennet

A new NMR method—requiring only milligram quantities of substrates—uses isotopically labeled neighbor atoms to directly and continuously report on KIEs at the reaction center. Application of the methodology defines a reaction coordinate for sialidase hydrolysis.

408  Reconstruction of the saframycin core scaffold defines dual Pictet-Spengler mechanisms
K Koketsu, K Watanabe, H Suda, H Oguri & H Oikawa

The chemical synthesis of acylated dipeptide substrates for SfmC, a tetradomain NRPS enzyme, defines the mechanism of formation of two rings in saframycin and demonstrates an unexpected role for a cryptic acyl chain in determining the reaction sequence.

ARTICLES

411  Metabolic oxidation regulates embryonic stem cell differentiation
O Yanes, J Clark, D M Wong, G J Patti, A Sánchez-Ruiz, H P Benton, S A Trauger, C Desponts, S Ding & G Siuzdak

Metabolomics analysis of stem cells and differentiated cells points to chemical unsaturation as a key feature of stem cell metabolites. Manipulation of these metabolites’ concentrations directly influences stem cell behavior, highlighting biological oxidation as a driver for differentiation.

418  In vitro bacterial polysaccharide biosynthesis: defining the functions of Wzy and Wzz
R Woodward, W Yi, Lei Li, G Zhao, H Eguchi, P R Sridhar, H Guo, J K Song, E Motari, L Cai, P Kelleher, X Liu, W Han, W Zhang, Y Ding, M Li & P G Wang

O-polysaccharide is a major constituent of the bacterial cell wall, yet little mechanistic information is known about its biosynthesis. A reconstruction of this pathway using defined substrates now demonstrates the basis for sugar polymerization and length modulation.

424  Endoplasmic reticulum Ca\(^{2+}\) increases enhance mutant glucocerebrosidase proteostasis
D S T Ong, T-W Mu, A E Palmer & J W Kelly

Enhancing calnexin function by increasing the ER calcium concentration resculpts the mutant glucocerebrosidase folding free energy diagram in the ER of Gaucher’s disease cells, enhancing folding at the expense of the ER-associated degradation pathway.

© 2010 Nature America, Inc. All rights reserved.
433  Cyclooxygenase-2 generates anti-inflammatory mediators from omega-3 fatty acids  
A L Groeger, C Cipollina, M P Cole, S R Woodcock, G Bonacci, T K Rudolph, V Rudolph, B A Freeman & F J Schopfer

Six new species of electrophilic lipids identified in activated macrophages are derived from COX-2 action on ω-3 fatty acids and mediate anti-inflammatory and anti-oxidant activities.

N&V p401

442  Rational design of small-molecule inhibitors of the LEDGF/p75-integrase interaction and HIV replication  
F Christ, A Voet, A Marchand, S Nicolet, B A Desimmie, D Marchand, D Bardiot, N J Van der Veken, B Van Remoortel, S V Strelkov, M De Maeyer, P Chaltin & Z Debyser

Interaction between HIV-1 integrase and the cellular cofactor LEDGF/p75 is important for viral integration. Newly designed small molecules that block this interaction inhibit HIV replication, illustrating the potential of viral–host protein–protein interaction inhibitors.

449  Small-molecule inhibition of APT1 affects Ras localization and signaling  

Reversible palmitoylation controls the localization and signaling of Ras. Development of a potent and specific small molecule inhibitor of the thioesterase APT1 reveals that this enzyme depalmitoylates Ras in cells. Inhibition of APT1 led to redistribution and altered activity of HRas, NRas and an oncogenic mutant Ras.

457  Small molecules discovered in a pathway screen target the Rho pathway in cytokinesis  
A B Castoreno, Y Smurnyy, A D Torres, M S Vokes, T R Jones, A E Carpenter & U S Eggert

A new pathway screen for small molecules that suppress or enhance an RNAi phenotype in Drosophila cells was used to identify a collection of compounds that perturb different steps in the Rho pathway.

N&V p397

464  Reprogramming bacteria to seek and destroy an herbicide  
J Sinha, S J Reyes & J P Gallivan

Synthetic biology enables the reprogramming of cells for useful applications. RNA selection approaches yielded an atrazine-binding riboswitch that was used to engineer Escherichia coli that migrate toward and catabolize this common herbicide.

N&V p398