RESEARCH HIGHLIGHTS
989 Our choices from the recent literature

NEWS AND VIEWS
990 Photosynthesis: Short circuit at the chlorophyll
Marc M Nowaczyk & Nicolas Plumeré
► Article p1046
991 Drug discovery: Doubling down on BET inhibition
Dafydd Owen
► Articles pp1089, 1097
993 Nuclear receptors: PPARα ligands make memories
Thomas P Burriss
► Article p1075

BRIEF COMMUNICATIONS
995 Cbr1 is a Dph3 reductase required for the tRNA wobble uridine modification
Z Lin, M Dong, Y Zhang, E A Lee & H Lin

A proteomic approach in Saccharomyces cerevisiae identifies cytochrome b reductase (Cbr1) as an NADH-dependent electron donor for diphthamide biosynthesis 3 (Dph3), a protein that serves as an electron source for diphthamide biosynthesis and tRNA modification.
998 Serine is a new target residue for endogenous ADP-ribosylation on histones
O Leidecker, J J Bonfiglio, T Colby, Q Zhang, I Atanassov, R Zaja, L Palazzo, A Stockum, I Ahel & I Matic
ADP-ribosylation is a post-translational protein modification that regulates numerous cellular pathways. An approach involving histone purification, partial filter-aided digestion and ETD mass spectrometry reveals that serine residues in histone proteins are ADP-ribosylated.

1001 Structural basis of nonribosomal peptide macrocyclization in fungi
J Zhang, N Liu, R A Cacho, Z Gong, Z Liu, W Qin, C Tang, Y Tang & J Zhou
Unlike their bacterial counterparts, fungal nonribosomal peptide synthetases utilize a terminal condensation-like (C_T) domain to form macrocycles, details of which are illuminated by structures of a C_T domain and neighboring thiolation domain.

1004 Discovery of MRSA active antibiotics using primary sequence from the human microbiome
The synthetic bioinformatic natural products (syn-BNPs) approach identifies putative natural products that are validated directly by independent synthesis. Its application led to the identification of humimycins, non-ribosomal peptides that have antimicrobial activity in mice.

ARTICLES

1007 Polyketide and nonribosomal peptide retrobiosynthesis and global gene cluster matching
C A Dejong, G M Chen, H Li, C W Johnston, M R Edwards, P N Rees, M A Skinnider, A L H Webster & N A Magarvey
Two programs, GRAPE and GARLIC, work together to first predict biosynthetic gene clusters responsible for the production of polyketides and nonribosomal peptides, then link sequenced gene clusters to known and unknown natural products.

1015 Functional mining of transporters using synthetic selections
H J Genee, A P Bali, S D Petersen, S Siedler, M T Bonde, L S Gronenberg, M Kristensen, S J Harrison & M O A Sommer
Functional annotation of bacterial thiamine transporters via a generalizable synthetic biology approach using riboswitches identifies a novel family of thiamine-uptake systems from prokaryotic metagenomes, including PnuT, as well as two novel xanthine importers.
1023 Oligosaccharyltransferase inhibition induces senescence in RTK-driven tumor cells
A high-throughput screen identifies NGI-1 as an inhibitor of oligosaccharyltransferase, preventing transfer of N-linked glycans to proteins. NGI-1 blocked EGFR signaling in non-small-cell lung cancer cell lines and promoted cell-cycle arrest and senescence.

1031 Enzymatic hydrolysis by transition-metal-dependent nucleophilic aromatic substitution
S Kalyoncu, D P Heaner Jr, Z Kurt, C M Bethel, C U Ukachukwu, S Chakravarthy, J C Spain & R L Lieberman
5-Nitroanthranilic acid aminohydrolase catalyzes the first step in biodegradation of a nitroaromatic compound via a nucleophilic aromatic substitution mechanism with an unusual substrate-assisted metal loading step.

1037 Nuclear receptors control pro-viral and antiviral metabolic responses to hepatitis C virus infection
A metabolomics analysis finds that host glycolysis, fatty acid oxidation, the urea cycle, cholesterol biosynthesis and oxidative phosphorylation are modified by hepatitis C virus infection. These effects are mediated through nuclear receptor transcription factors HNF4α, PPARα and FXR.

1046 Competing charge transfer pathways at the photosystem II–electrode interface
J Z Zhang, K P Sokol, N Paul, E Romero, R van Grondelle & E Reisner
When coupled to electrodes, the photosystem II complex can participate in a photo-induced oxygen reduction mechanism via chlorophyll a pigments that competes against the desired water-oxidation charge transfer pathway.

1053 SF2312 is a natural phosphonate inhibitor of enolase
SF2312, a phosphonate antibiotic, directly binds and inhibits the activity of the glycolytic enzyme enolase 2 (ENO2) in cells and is selectively toxic to ENO1-deleted glioma cells through inhibition of glycolysis and depletion of ATP.
1059  A photoactivatable Cre–loxP recombination system for optogenetic genome engineering
F Kawano, R Okazaki, M Yazawa & M Sato

The Cre–loxP recombination system is a classical tool for targeted genetic engineering. Blue-light-induced dimerization of a split Cre system enables efficient light-controlled DNA integration at loxP sites within cells and in living mouse tissues.

1065  Structural and conformational determinants of macrocycle cell permeability
B Over, P Matsson, C Tyrchan, P Artursson, B C Doak, M A Foley, C Hilgendorf, S E Johnston, M D Lee IV, R J Lewis, P McCarren, G Muncipinto, U Norinder, M W D Perry, J R Duvall & J Kihlberg

Detailed computational and structural analysis of a large data set of non-peptidic macrocycles revealed particular functional groups, substituents and molecular properties that are critical for dictating cellular permeability.

1075  Identification and characterization of PPARα ligands in the hippocampus
A Roy, M Kundu, M Jana, R K Mishra, Y Yung, C-H Luan, F J Gonzalez & K Pahan

Three endogenous ligands of the nuclear receptor PPARα—hydroxydimethylbutyrate, hexadecanamide, and octadecenamide—are potentially responsible for noncanonical activity of PPARα in synaptic function and hippocampal plasticity.

1084  A prevalent intraresidue hydrogen bond stabilizes proteins
R W Newberry & R T Raines

Within polypeptides, C5 hydrogen bonds form between the amide proton and carbonyl oxygen of the same residue. This intraresidue interaction stabilizes β-sheets in particular and is widespread throughout structurally characterized proteins.

1089  Design and characterization of bivalent BET inhibitors
M Tanaka, J M Roberts, H-S Seo, A Souza, J Paulk, T G Scott, S L DeAngelo, S Dhe-Paganon & J E Bradner

Targeting the acetyllysine ‘reader’ activity of BET-family transcriptional coactivators has emerged as an anticancer modality. A new class of dimeric JQ1 derivatives displays enhanced potency for bivalent targeting of tandem bromodomains in BET proteins.
1105 Small-molecule factor D inhibitors targeting the alternative complement pathway

A fragment-based design approach identifies reversible inhibitors targeting human protease complement factor D (FD), which is required for amplification of complement C3 signaling. FD inhibitors act as systemic regulators of complement activation in vivo.

1111 Selective recognition of histone crotonylation by double PHD fingers of MOZ and DPF2
X Xiong, T Panchenko, S Yang, S Zhao, P Yan, W Zhang, W Xie, Y Li, Y Zhao, C D Allis & H Li

Structural and biophysical analysis of the histone acetyltransferase MOZ double PHD finger (DPF) domain reveal that DPF exhibits strong binding preference for crotonylated Lys14 in histone H3 (H3K14) and are co-localized in cells.