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631 Postgenomic chemical biology

RESEARCH HIGHLIGHTS
632 Our choices from the recent literature

NEWS AND VIEWS
634 Post-translational modifications: A shift for the O-GlcNAc paradigm
Jennifer J Kohler
► Article p645

636 Metalloenzymes: Natural product nitrosation
Roland D Kersten & Pieter C Dorrestein
► Brief Communication p641

637 Chemical ecology: Reprogramming a termite monarchy
Jennifer J Buswell & Leslie B Vosshall

639 Screening: Your brain on drugs
Jonathan P Saxe

BRIEF COMMUNICATION
641 A copper-containing oxidase catalyzes C-nitrosation in nitrosobenzamide biosynthesis
A Noguchi, T Kitamura, H Onaka, S Horinouchi & Y Ohnishi

A variety of natural C-nitroso compounds are known, but the path to these important functional groups has been a mystery. Elucidation of the biosynthetic route to an iron chelator now reveals a tyrosinase-like copper-containing monooxygenase as responsible for the transformation.
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ON THE COVER
Post-translational modifications
Counting carbs
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Biotin biosynthesis
Surprise substrates
Article p682

Drug discovery
Beyond bisphosphonates
Article p660

COVER IMAGE
Zinc ions are important signaling agents in oocyte maturation. Total zinc content increases in maturing oocytes, and zinc insufficiency causes meiotic arrest midway through reductive division with the spindle apparatus stalled at telophase I. The cover pictures a cell that is arrested in telophase I and stained for α-tubulin (magenta), F-actin (green) and DNA (yellow). Cover art by Erin Boyle, based on artwork provided by Alison Kim. Article p674
645  Quantification of O-glycosylation stoichiometry and dynamics using resolvable mass tags
J E Rexach, C J Rogers, S-H Yu, J Tao, Y E Sun & L C Hsieh-Wilson

Current methods to investigate glycosylation allow the identification of modification sites but provide limited additional information. A new strategy using polymers to label specific sugars now shows a huge variety in the occupancy of known glycosylation sites as well as unexpected interplay between post-translational modifications.

▶ N&V p634

652  Replication-dependent instability at (CTG)•(CAG) repeat hairpins in human cells
G Liu, X Chen, J J Bissler, R R Sinden & M Leffak

Instability of (CTG)•(CAG) repeats in microsatellite DNA has been linked to numerous neurological diseases. Probing trinucleotide repeat structures using engineered zinc-finger nucleases provides evidence that DNA hairpins form in vivo and are linked to replication-dependent genomic instability.

660  Allosteric non-bisphosphonate FPPS inhibitors identified by fragment-based discovery

Although FPPS is a potential anti-cancer target, the high bone affinity of nitrogen-containing bisphosphonates, FPPS inhibitors used clinically to treat bone disease, has prevented their development as cancer therapeutics. Using fragment-based drug discovery, non-bisphosphonate inhibitors were discovered that bind in a previously undescribed allosteric pocket.

667  A small-molecule inhibitor shows that pirin regulates migration of melanoma cells
I Miyazaki, S Simizu, H Okumura, S Takagi & H Osada

A chemical array screen identifies a small-molecule inhibitor of pirin that inhibits its interaction with the oncoprotein Bcl3 and decreases the expression of the tumor mobility protein SNAI2. As a result, the compound perturbs the migration of melanoma cells that have high pirin expression levels.

674  Zinc availability regulates exit from meiosis in maturing mammalian oocytes
A M Kim, S Vogt, T V O’Halloran & T K Woodruff

Probing the biological location and function of transition metals has proven difficult. X-ray fluorescence microscopy in combination with an array of metal chelators now provides a way to interrogate zinc in maturing mouse oocytes, demonstrating a role for this metal in cell division.
Biotin synthesis begins by hijacking the fatty acid synthetic pathway
S Lin, R E Hanson & J E Cronan

Biotin synthesis is known to include a pimelate intermediate, the construction of which is controversial. Genetic manipulations and chemical feeding now demonstrate that the two mystery enzymes in the process create and cleave a methyl ester that sends a biotin precursor into the fatty acid synthesis machinery.

CORRECTIONS

ERRATA