Discovery of a stapled peptide inhibitor of Mcl-1. Stewart et al. screened a library of stapled peptides based on the BH3 domains of BCL-2 family proteins (library depicted on left) and identified a selective inhibitor of MCL-1 (structure of the inhibitor in complex with Mcl-1 shown on the right), one of the anti-apoptotic family members that plays a key role in the survival of cancer cells. The peptide inhibitor, derived from the BH3 domain of MCL-1 itself, sensitizes cancer cells to caspase-dependent apoptosis, providing a novel tool to study and modulate this potential drug target.

Cover art by Erin Boyle, based on artwork provided by Eric D. Smith.

Article p595; News & Views p566
581 An ATP-independent strategy for amide bond formation in antibiotic biosynthesis
M Funabashi, Z Yang, K Nonaka, M Hosobuchi, Y Fujita, T Shibata, X Chi & S G Van Lanen

Amide bonds are routinely formed in biological systems using carboxylic acids that have been activated at the expense of ATP. The biochemical characterization of a putative β-lactamase now reveals a new way to form amide bonds using stable methyl ester intermediates.

587 Time-resolved FRET between GPCR ligands reveals oligomers in native tissues

Evidence for the existence and importance of GPCR dimers and oligomers is mounting, but direct detection of these species has been challenging. The development of improved fluorescent ligands for time-resolved spectroscopy confirms their presence across GPCR families and in native tissue.

595 The MCL-1 BH3 helix is an exclusive MCL-1 inhibitor and apoptosis sensitizer
M L Stewart, E Fire, A E Keating & L D Walensky

MCL-1 has emerged as a major oncogenic and chemoresistance factor. A screen of stapled peptide helices identified the MCL-1 BH3 domain as selectively inhibiting MCL-1 among the related anti-apoptotic Bcl-2 family members, providing insights into the molecular determinants of binding specificity and a new approach for sensitizing cancer cell apoptosis.

602 Iron traffics in circulation bound to a siderocalin (Ngal)–catechol complex

The lipocalin protein Scn-Ngal is known to bind iron-chelating siderophores, leading to inhibition of bacterial growth. New results reveal that Scn-Ngal, in the absence of bacterial infection, can form a complex with catechol that binds and transports iron in vivo.
610  Palmitoylome profiling reveals S-palmitoylation-dependent antiviral activity of IFITM3
J S Yount, B Moltedo, Y-Y Yang, G Charron, T M Moran, C B López & H C Hang

Proteomic analysis in dendritic cells identifies three palmitoylation sites within IFITM3, an innate immunity protein involved in inhibition of early replication of several viruses. Palmitoylation of IFITM3 regulates its clustering in membranes and is crucial for inhibition of influenza virus infection.

615  n→π* interactions in proteins
G J Bartlett, A Choudhary, R T Raines & D N Woolfson

Proteins rely on a combination of intramolecular forces to form and stabilize their structures. A careful comparison of computational analysis and high-resolution crystal structures now indicates that the n→π* interaction merits inclusion in this group.

► N&S v p567

621  Transcriptional regulation by small RNAs at sequences downstream from 3' gene termini
X Yue, J C Schwartz, Y Chu, S T Younger, K T Gagnon, S Elbashir, B A Janowski & D R Corey

Small RNAs targeted to gene promoters are known regulators of transcription in mammalian cells. Antigene RNAs complementary to non-coding transcripts localized to the 3' termini of genes are now shown to regulate transcription across long genomic sequences.

CORRECTIONS

630  ERRATA

CLASSIFIEDS

See the back pages