COVER IMAGE
With the June 2015 issue, *Nature Chemical Biology* celebrates 10 years of serving the chemical biology community through the publication of leading research and commentary at the interface of chemistry and biology. The cover features art created by Mary O’Reilly, the winner of our “10th Anniversary Cover Art Competition,” and shows a bursting piñata revealing the molecular bounty of chemical biology. Art direction by Erin Dewalt.

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The use of ene adducts to study and engineer enoyl-thioester reductases
R G Rosenthal, B Vögeli, N Quade, G Capitani, P Kiefer, J A Vorholt, M-O Ebert & T J Erb

The use of a presumed chemical intermediate in the mechanism of enoyl-thioester reductase enables the identification of the long-sought proton donor and the rational redesign of enzyme stereoselectivity.

Mode of action and pharmacogenomic biomarkers for exceptional responders to didemnin B

The natural product didemnin B inhibits PPT1 and the antiapoptotic protein Mcl-1 in particular types of cancer cells containing a unique genetic profile that correlates with drug sensitivity.

Catalytic mechanism of a retinoid isomerase essential for vertebrate vision
P D Kiser, J Zhang, M Badiee, Q Li, W Shi, X Sui, M Golczak, G P Tochtrop & K Palczewski

Retinoid isomerase is a critical enzyme in the conversion of retinyl esters to 11-cis-retinal, a key step in the regeneration of visual pigments that mediate light perception. Structural, biochemical and modeling data using substrate analogs explain how this unusual reaction proceeds.

Translating slow-binding inhibition kinetics into cellular and in vivo effects

Drug-target residence time is viewed as a predictor of the clinical efficacy of small-molecule drugs. A pharmacodynamic model, taking into account the target binding kinetics of antibacterial compounds, leads to accurate predictions of cellular and in vivo efficacies of the inhibitors.
HIV gp41-mediated membrane fusion occurs at edges of cholesterol-rich lipid domains
S-T Yang, V Kiessling, J A Simmons, J M White & L K Tamm

Fusion of HIV with target membranes via the HIV fusion peptide requires phase separation among lipids as well as phase heterogeneity because the fusion is biased toward the boundary between regions of ordered (so-called rafts) and disordered lipids.
▶ N&V p383

A selective inhibitor of PRMT5 with in vivo and in vitro potency in MCL models

Protein methyltransferase PRMT5 symmetrically dimethylates arginine residues in proteins, including histones, and has been associated with tumorigenesis. The identification of EPZ015666 as a potent chemical probe of PRMT5 could promote understanding of the role of PRMT5 in human disease both in cells and in vivo.