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**Next Due Date:** Monday, May 15, 2017

## Instructions for Authors (Volume 1)

Identify articles to abstract in the journals you have been assigned. Try to pick things that the group (or specific subgroups) would like to read or should be aware of. This does not need to be limited to chemistry! If you encounter interesting pieces of media elsewhere (The Economist being a recent example) don't hesitate to let the group know. If you are splitting a journal with another group member, talk with him/her to be sure you are not reviewing redundantly. If you are not able to cover your journal for some reason, get someone to cover it for you—as if it were your group job.

### Create an Abstract

Abstract submissions are usually prepared using ChemDraw. The editors of the *Lit Review* strongly encourage the copying of graphical material from PDF files and wish to point out the following. Graphics stored in PDF files are typically of postscript or >300 dpi quality. When an image is copied into a ChemDraw document, a screen snapshot is taken, and the image is captured at the present screen resolution. If the PDF file is being viewed zoomed-in, this typically results in the transfer of a high quality image. If the PDF is being viewed zoomed-out, a low quality image typically results. Text can be copied from a PDF file and pasted as text using the text select or column select tool. Once pasted, this text behaves as if it were input from the keyboard.

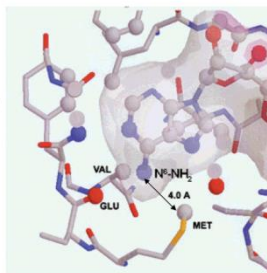
Include a brief textual summary of the article; an example of a completed abstract is shown below. The list of topics and subgroups on the right is useful to highlight which subgroups should pay attention to your abstract and roughly what kind of chemistry the article contains.

Please email the files to knear@stanford.edu. Late abstracts will be included in the Lit Review for the following month. **PCs please send .cdx and macs please send .pdf files.**

Citation: Abeyweera, T.P.; Rotenberg, S.A. *Biochemistry* 2007, 46, 2364-2370

#### Design and Characterization of a Traceable Protein Kinase C-alpha

Protein kinase CR (PKCR) is a critical component of pathways that govern cancer-related phenotypes such as invasion and proliferation. Proteins that serve as immediate substrates for PKCR offer potential targets for anticancer drug design. To identify specific substrates, a mutant of PKCR (M417A) was constructed at the ATP binding site such that it could bind a sterically large ATP analogue derivatized through the N6 amino group of adenosine (1- $\beta$ -<sup>32</sup>P-N6-phenyl-ATP). Because this analogue could be utilized by the mutant kinase but not by wild-type PKCR (or presumably other protein kinase) to phosphorylate peptide or protein substrates, <sup>32</sup>P-labeled products were the direct result of the mutant PKCR.



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Citation: Dictionary.com (search term = "mook")

For those of you who always wanted to know what it meant....

**mook** **Pronunciation Key** (mk) *n. Slang*

An insignificant or contemptible person.

*methods*  
synthesis

### DON'T BE A MOOK!

Lit Review MOOKS include those who:

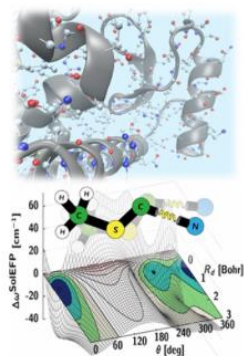
- fail to submit their abstracts in a timely fashion (or at all), or
- claim there was nothing to abstract in *JACS*, *JOC*, *Org. Lett.*, etc.

Penalties for being a Lit Review MOOK:

- You will get last choice when it's time to pick new journals.

Citation: Cho *et al. Acc. Chem. Res.* **2017**, ASAP

### Vibrational Probes: From Small Molecule Solvatochromism Theory and Experiments to Applications in Complex Systems

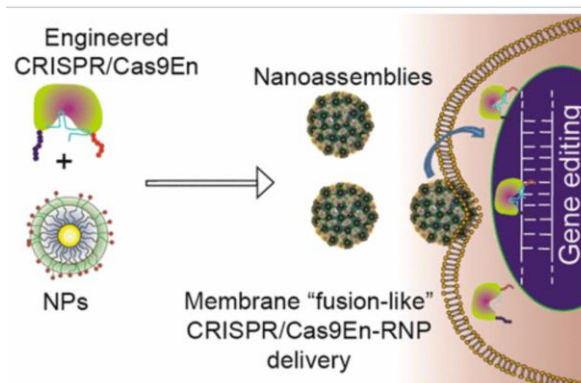


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 Prostratin

Citation: Mout, R. *et al. ACS Nano*, **2017**, 11 (3) 2452-2458

### Direct Cytosolic Delivery of CRISPR/Cas9-Ribonucleoprotein for

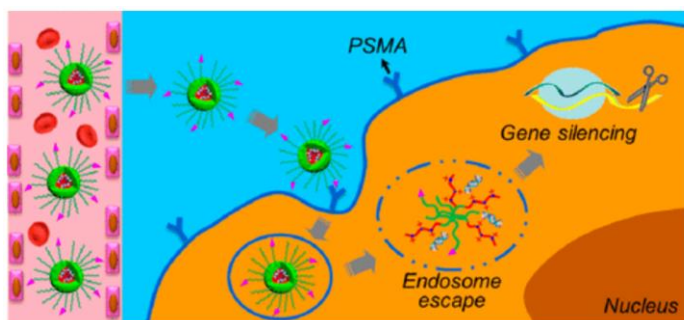


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Citation: Xu, X. *et al. ACS Nano*, **2017**, 11 (3) 2618-2627

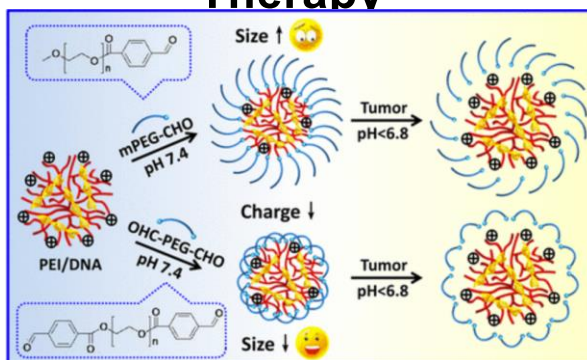
### Multifunctional Envelope-Type siRNA Delivery Nanoparticle Platform for Prostate Cancer Therapy



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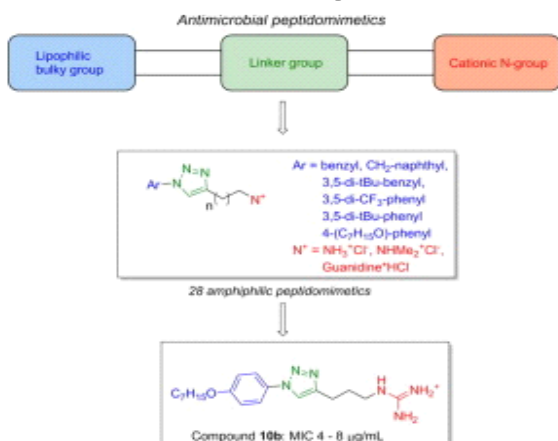
## A pH-Responsive Detachable PEG Shielding Strategy for Gene Delivery System in Cancer Therapy



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## Synthesis and antimicrobial evaluation of cationic low molecular weight amphipathic 1,2,3-triazoles

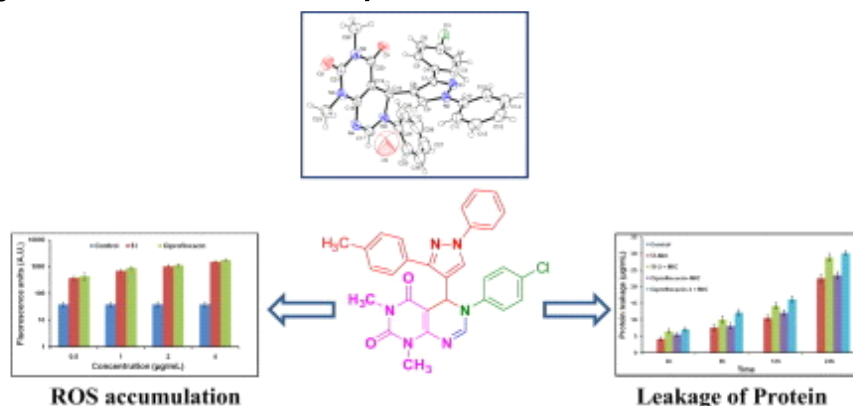


A library of 28 small cationic 1,4-substituted 1,2,3-triazoles was prepared for studies of antimicrobial activity. Eight compounds showed promising antimicrobial activity, of which the most potent compound 10b displayed minimum inhibitory concentrations of 4–8 µg/mL against *Streptococcus agalacticae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Enterococcus faecalis*.

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## Design, synthesis and evaluation of novel pyrazolo-pyrimido[4,5-d]pyrimidine derivatives as potent antibacterial and biofilm inhibitors

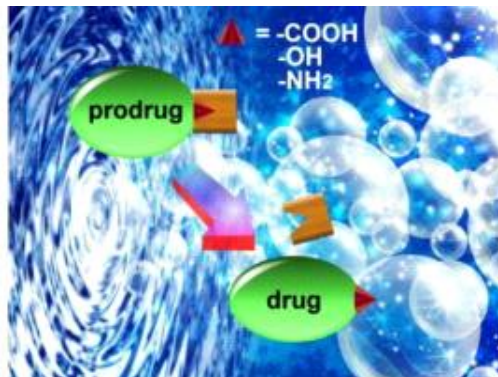


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Citation: Hamada, Y. *Bioorg. Med. Chem. Lett.* **2017**, 27, 1627.

### Recent progress in prodrug design strategies based on generally applicable modifications



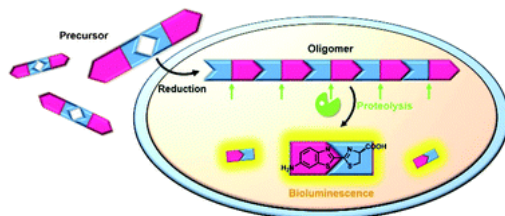
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Citation: Zheng, Z.; *et al. Chem Commun.* **2017**, 53, 3567.

### Intracellular synthesis of D-aminoluciferin for bioluminescence generation

D-Luciferin is the most widely used substrate for bioluminescence (BL) applications but its low chemical stability always affects its performance. The authors rationally designed two chemically stable precursor molecules CBT-D-cystine-CBT (D-1) and CBT-L-cystine-CBT (L-1), and subjected them to reduction-controlled condensation to form 1-oligomer and subsequent proteolysis to yield D-aminoluciferin for BL generation in cells and in vivo. These precursor molecules might serve as D-luciferin alternatives for a wide range of BL applications in the near future.

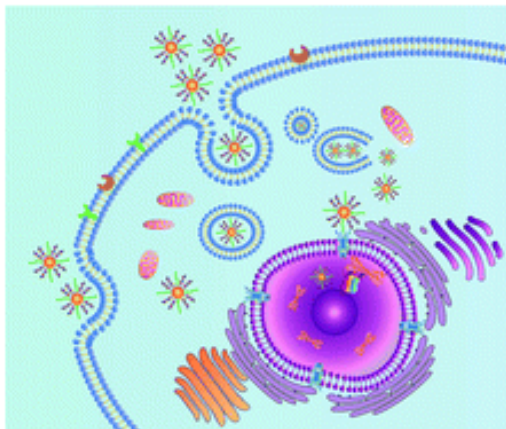


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Citation: Li, N.; *et al. Chem. Sci.* **2017**, 8, 2816

### Nuclear-targeted siRNA delivery for long-term gene silencing

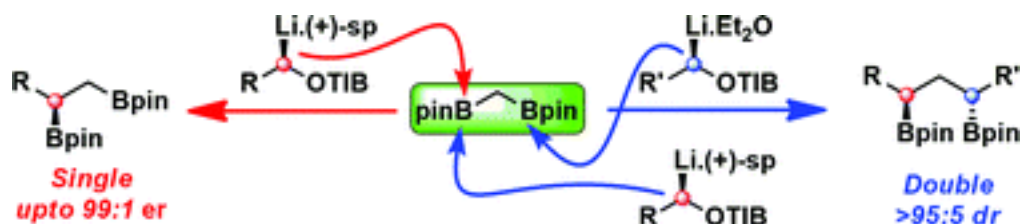


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Citation: Blair, D. J.; et al. *Chem. Sci.* **2017**, 8, 2898

### Selective uni- and bidirectional homologation of diborylmethane

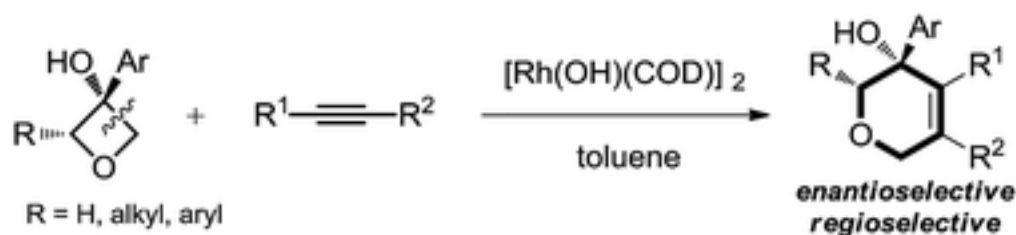


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Citation: Guo, R.; et al. *Chem. Sci.* **2017**, 8, 3002

### Rhodium(I)-catalyzed stereoselective [4+2] cycloaddition of oxetanols with alkynes through C(sp<sup>3</sup>)-C(sp<sup>3</sup>) bond cleavage

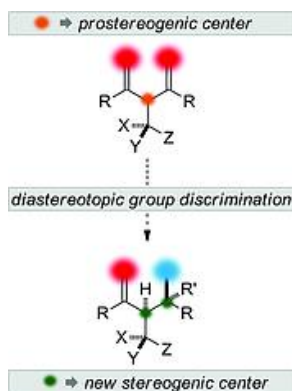


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Citation: Horwitz, M. A. et al. *Eur. J. Org. Chem.* **2017**, 11, 1381

### Local Desymmetrization through Diastereotopic Group Selection: An Enabling Strategy for Natural Product Synthesis

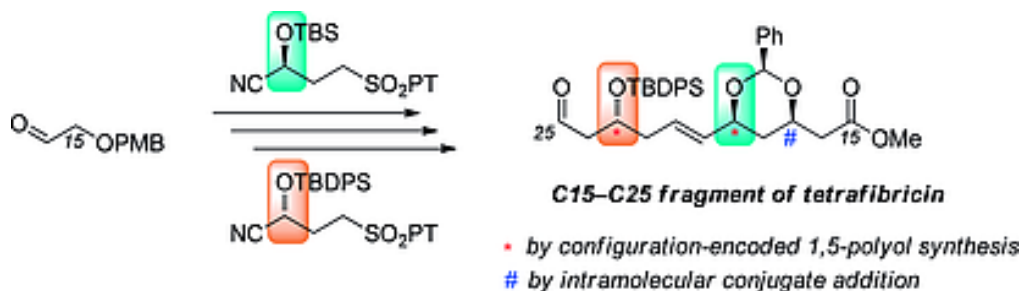


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Citation: Friedrich, R. M. et al. *Eur. J. Org. Chem.* **2017**, 14, 1961

### Access to an *anti,syn*-1,5,7-Triol by Configuration-Encoded 1,5-Polyol Synthesis: The C15-C25 Fragment of Tetrafrabricin

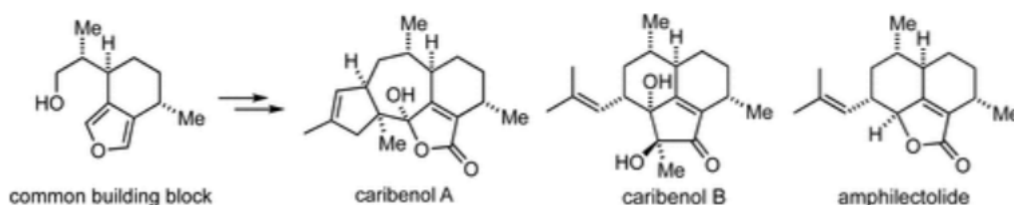


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Citation: *JACS*, **2017**, 139, 4117.

### Furans as Versatile Synthons: Total Syntheses of Caribenol A and Caribenol B



The syntheses feature a Friedel-Crafts triflation, a late-stage oxidation of a furan ring, an intramolecular organocatalytic alpha-arylation, and a nucleophilic addition to a hydroxy 1,2-diketone.

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Citation: *JACS*, **2017**, 139, 4584.

### Smart Nanostructures for Cargo Delivery: Uncaging and Activating by Light

Nanoplatforms that can be activated by an external application of light can be used for a wide variety of photoactivated therapies, especially light-triggered drug delivery systems, relying on photoisomerization, photo-cross-linking/un-cross-linking, photoreduction, and so forth. Light-activated nanomedicines and drug delivery systems are expected to provide more effective therapies against serious diseases such as cancers, inflammation, infections, and cardiovascular disease with reduced side effects and will open new doors toward the treatment of patients worldwide.

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Citation: **JAMA. 2017;317(14):1409-1410. doi:10.1001/jama.2017.1475**

**Achieving Universal Coverage Without Turning to a Single Payer: Lessons From 3 Other Countries**

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Citation: Hoque, et al. *Mor. Pharm.* **2017, 14**, 1218-1230

**Biocompatible Injectable Hydrogel with Potent Wound Healing and Antibacterial Properties**

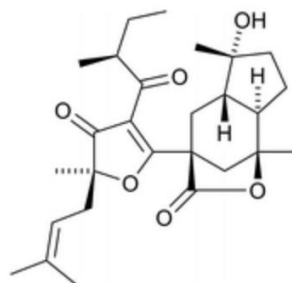
commonly used sealants typically lack antibacterial properties. Since bacterial infection at the wound site is very common, bioadhesive materials with intrinsic antibacterial properties are urgently required. Herein, we report a biocompatible injectable hydrogel with inherent bioadhesive, antibacterial, and hemostatic capabilities suitable for wound sealing applications. The hydrogels were developed in situ from an antibacterial polymer, N-(2-hydroxypropyl)-3-trimethylammonium chitosan chloride (HTCC), and a bioadhesive polymer, polydextran aldehyde. The gels were shown to be active against both Gram-positive and Gram-negative bacteria, including drug-resistant ones such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus faecium* (VRE), and  $\beta$ -lactam-resistant *Klebsiella pneumoniae*. Mechanistic studies revealed that the gels killed bacteria upon contact by disrupting the membrane integrity of the pathogen. Notably, the gel showed negligible toxicity toward human red blood cells (only 2% hemolysis) and no inflammation to the surrounding tissue upon subcutaneous implantation in mice, thus proving it as a safe and effective antibacterial sealant.

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Citation: Hill, R. et al. *Nat. Prod. Rep.*, **2017**, 34, 338-342

A personal selection of 32 recent papers is presented covering various aspects of current developments in bioorganic chemistry and novel natural products such as furanmonogone A from *Hypericum monoavnum*.



Furanmonogone A

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Citation: *Nature* **543**, 467 (23 March 2017) doi:10.1038/543467e

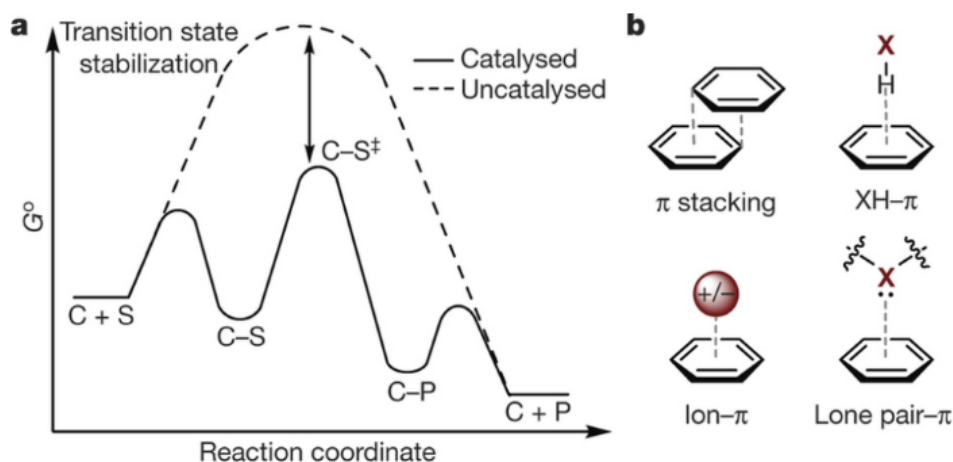
## CRISPR finds drug synergy

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Citation: *Nature* **543**, 637–646 (30 March 2017) doi:10.1038/nature21701

## Exploiting non-covalent $\pi$ interactions for catalyst design

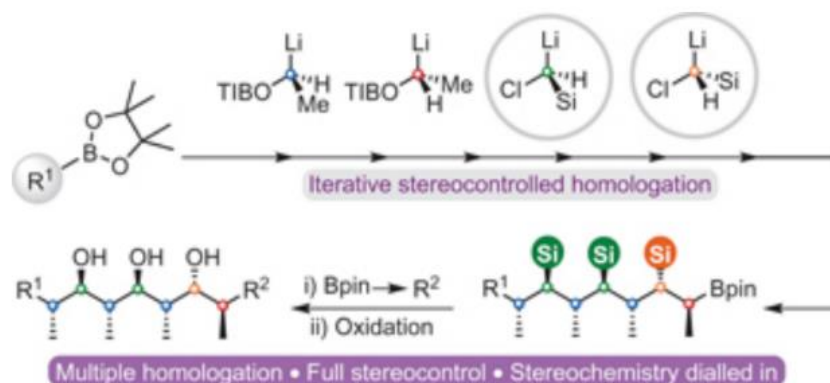


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Citation: *Nature Chemistry* (2017) doi:10.1038/nchem.2757

## Iterative assembly line synthesis of polypropionates with full stereocontrol

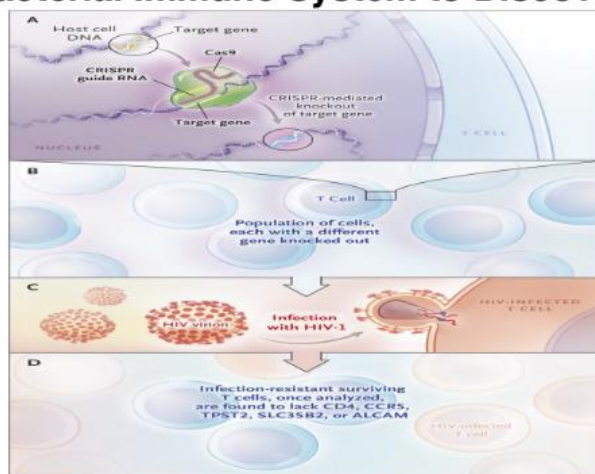


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Citation: *N Engl J Med* 2017; 376:1290-1291

## Repurposing a Bacterial Immune System to Discover Antiviral Targets

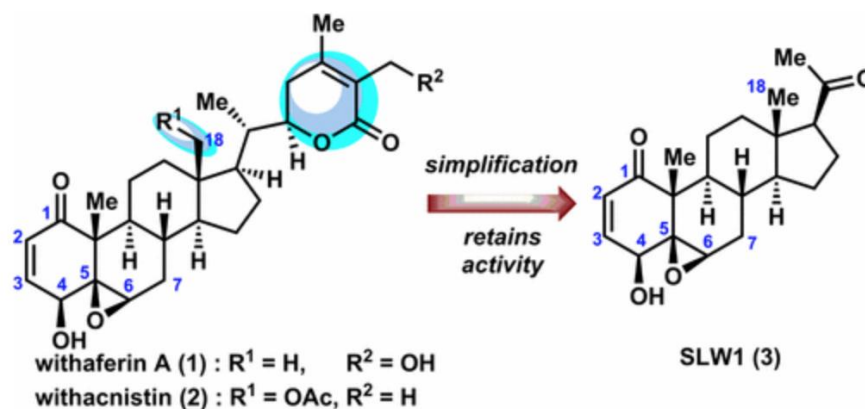


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Citation: Shair *et al. Org. Lett.* 2017, 19(7), 1538–1541

## STAT3 Inhibitory Activity of Structurally Simplified Withaferin A Analogues

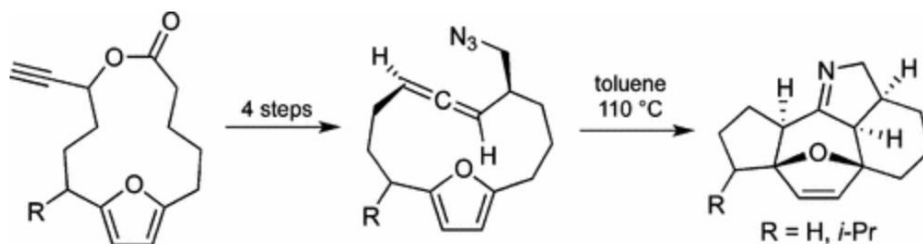


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Citation: Robertson *et al. Org. Lett.* 2017, ASAP

## Access to a Guanacastepene and Cortistatin-Related Skeleton via Ethynyl Lactone Ireland–Claisen Rearrangement and Transannular (4 + 3)-Cycloaddition of an Azatrimethylenemethane Diyl



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Citation: Haynes, *et al. Science*. **2017**, *355*, 1129-1130

### Developing an HIV vaccine

In 2015, 17 million HIV-infected individuals worldwide were on antiretroviral drug therapies, which are remarkably effective in suppressing the virus. Yet, 6000 people a day became newly infected, making the quest for an effective and safe HIV vaccine a major global priority. From 1987 to 2013, all of the six HIV vaccine efficacy trials failed except for one. The RV144 trial in Thailand that used a viral vector prime (expressing three HIV genes, env, gag, and pro) and a boost with HIV's glycoprotein gp120 (a constituent of the viral spike) showed a modest estimated 31.2% vaccine efficacy at 42 months. Although the RV144 trial showed putative short-lived vaccine efficacy, it was not sufficient for vaccine deployment. Nonetheless, from RV144 (1) and studies in animal models (2), a hypothesis gained. New trials have been designed to improve RV144 vaccine efficacy by using new adjuvants and Env proteins (1). Thus, one track of vaccine development is to investigate easy-to-induce, non-neutralizing antibodies that have FcR-mediated anti-HIV effector functions in vitro for their ability to prevent HIV transmission in vivo.

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Citation: Dawson, M.A.. *Science*. **2017**, *355*, 1147-1152

### The cancer epigenome: Concepts, challenges, and therapeutic opportunities

Cancer biology is profoundly influenced by changes in the epigenome. Because the dynamic plasticity of the epigenome lends itself well to therapeutic manipulation, the past few years have witnessed an unprecedented investment in the development, characterization, and translation of targeted epigenetic therapies. In this review, the author provide a broad context for recent developments that offer a greater understanding of how epigenetic regulators facilitate the initiation, maintenance, and evolution of cancer. He discuss newly developed epigenetic therapies and the cellular and molecular mechanisms that may govern sensitivity and resistance to these agents. He also review the rationale for future combination therapies involving existing and emerging epigenetic drugs.

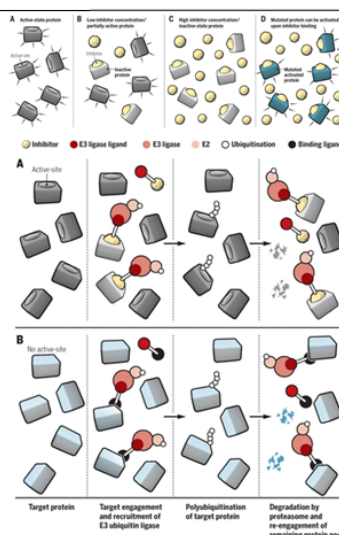
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Citation: Salami, *et al. Science*. **2017**, *355*, 1163-1167

### Waste disposal-An attractive strategy for cancer therapy

Although many of cancer drugs are effective in cancer patients, the response is often not durable because tumor cells develop resistance to the drugs. Another limitation of this strategy is that not all oncogenic driver proteins are druggable enzymes or receptors with activities that can be inhibited. Here we describe an alternative approach to targeted therapy that is based on co-opting the cellular quality-control machinery-the ubiquitin-proteasome system-to remove specific cancer-causing proteins from the cell. We first discuss examples of existing cancer drugs that work by degrading specific proteins and then review recent progress in the rational design and preclinical testing of small molecules that induce selective degradation of specific target proteins.



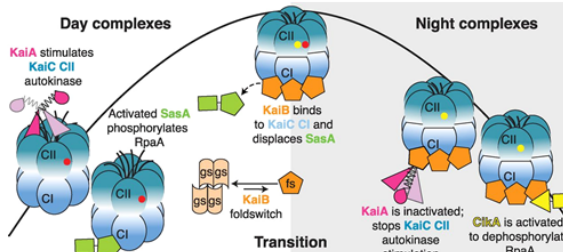
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Citation: Tseng, *et al. Science*. **2017**, *355*, 1174-1180.

### Structural basis of the day-night transition in a bacterial circadian clock

In cyanobacteria, timing is generated by a posttranslational clock consisting of KaiA, KaiB, and KaiC proteins and a set of output signaling proteins, SasA and CikA, which transduce this rhythm to control gene expression. Here, we describe crystal and nuclear magnetic resonance structures of KaiB-KaiC, KaiA-KaiB-KaiC, and CikA-KaiB complexes. They reveal how the metamorphic properties of KaiB, a protein that adopts two distinct folds, and the post-Cadenosine triphosphate hydrolysis state of KaiC create a hub around which nighttime signaling events revolve, including inactivation of KaiA and reciprocal regulation of the mutually antagonistic signaling proteins, SasA and CikA.



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Citation: Blondiaux, *et al. Science*. **2017**, *355*, 1206-1211

### Reversion of antibiotic resistance in *Mycobacterium tuberculosis* by spiroisoxazoline SMART-420

The development of drug resistance especially rifampicin resistance (RR), multidrug resistance (MDR) and extensive drug resistance (XDR) is particularly worrisome for tuberculosis (TB) (3). Approximately 580,000 MDR/RR-TB cases have occurred in 2015, resulting in about 250,000 deaths. Some of the most effective anti-TB antibiotics require bioactivation by *Mycobacterium tuberculosis* enzymes to acquire their antibacterial effect. These pro-antibiotics not only include the 40-year-old compounds isoniazid (INH), pyrazinamide (PZA), p-aminosalicylic acid (PAS) and ethionamide (ETH), but also the recently approved drug delamanid (OPC-67683) and the under-clinical-evaluation compound pretomanid (PA824). However, bioactivation of pro-antibiotics is vulnerable to mutational inactivation or attenuation of the corresponding bioactivating enzymes, as observed for INH-, PZA-, and ETH-resistant clinical isolates with mutations in *katG* (8), *pncA* (9), and *ethA* (10, 11), respectively. The authors have developed drug-like molecules that activate a cryptic alternative bioactivation pathway of ethionamide in *M. tuberculosis*, circumventing the classic activation pathway in which resistance mutations have now been observed. The first-of-its-kind molecule, named SMART-420 (Small Molecule Aborting Resistance), not only fully reverses ethionamide-acquired resistance and clears ethionamide-resistant infection in mice, it also increases the basal sensitivity of bacteria to ethionamide. The bioactivation of ETH in *M. tuberculosis* is normally catalyzed by the Baeyer-Villiger monooxygenase EthA (10, 11, 16). Transformation of ETH by EthA into highly reactive intermediates leads to the formation of a stable covalent adduct of ETH and nicotinamide adenine dinucleotide (NAD) (10, 17). This adduct binds to and inhibits the enoyl reductase *InhA* involved in mycolic acid biosynthesis, one of the essential components in the mycobacterial cell wall

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### Dengue may bring out the worst in Zika

antibody-dependent enhancement (ADE) is a well-known phenomenon with dengue, which has four serotypes that infect humans. Infection with one dengue serotype typically causes little harm, but the antibodies produced against it can set people up for severe and even deadly disease if they subsequently become infected by a different serotype. Dengue, West Nile, and Zika are all from the flavivirus family and the researchers warn that a vaccine against one could put a person at risk for ADE from a relative. Dengue is closest to Zika, and indeed the mouse experiment showed that dengue antibodies led to the most severe Zika disease. ADE also led to high levels of virus in mouse testes and spinal cords, which may help explain sexual transmission of Zika in humans and central nervous system diseases like microcephaly in babies and Guillain-Barr Syndrome in adults.

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