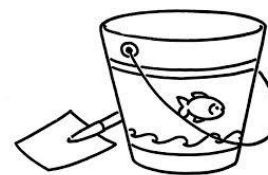


Volume 42 / Issue 8 15 August 2017



Accounts of Chemical Research	MOOK	Quang Luu-Nguyen
ACS Central Science	MOOK	Colin McKinlay
ACS Chemical Biology	MOOK	Clayton Hardman
ACS Nano	103	Nancy Benner
Advanced Drug Delivery Reviews	N/A	N/A
Angewandte Chemie International Edition	N/A	N/A
Bioconjugate Chemistry	N/A	N/A
Biomacromolecules	103	Nancy Benner
Bioorganic and Medicinal Chemistry	N/A	N/A
Bioorganic and Medicinal Chemistry Letters	N/A	Katie Near
Chemical Communications	103	Katie Near
Chemical & Engineering News	MOOK	Colin McKinlay
Chemical Reviews	MOOK	Jefferson Tyler
Chemical Science	MOOK	Jack Sloane
Chemistry, A European Journal	MOOK	Clayton Hardman
European Journal of Organic Chemistry	MOOK	Jack Sloane
Journal of the American Chemical Society	MOOK	Melanie Huttner (odd)
		Akira Shimizu (even)
JAMA	104	Stephen Ho
Journal of Medicinal Chemistry	N/A	N/A
Journal of Organic Chemistry	N/A	N/A
Molecular Pharmaceutics	105	Xiaoyu Zang (Janice)
Natural Product Reports	105	Nancy Benner
Nature	106	Stephen Ho
Nature Chemistry	106	Stephen Ho
Nature Chemical Biology	107	Xiaoyu Zang (Janice)
New England Journal of Medicine	108	Stephen Ho
The New York Times	N/A	N/A
The Onion	N/A	N/A
Organic Letters	MOOK	Quang Luu-Nguyen
Organometallics	N/A	N/A
PNAS	MOOK	Colin McKinlay
Science	108	Xiaoyu Zang (Janice)
Science Translational Medicine	MOOK	Jefferson Tyler
Synlett	N/A	N/A
Synthesis	N/A	N/A
Tetrahedron	N/A	N/A
Tetrahedron Letters	N/A	N/A

Next Due Date: Friday, September 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.

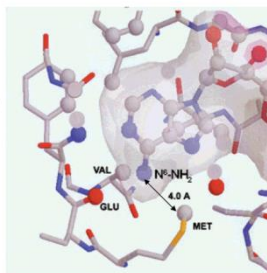
Include a brief textual summary of the article; an example of a completed abstract is shown below. The list of topics and subgroups on the right is useful to highlight which subgroups should pay attention to your abstract and roughly what kind of chemistry the article contains.

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- β - 32 P- γ -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, 32 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.

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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: Dengfeng, H. et al. *ACS Nano*, 2017, Just accepted

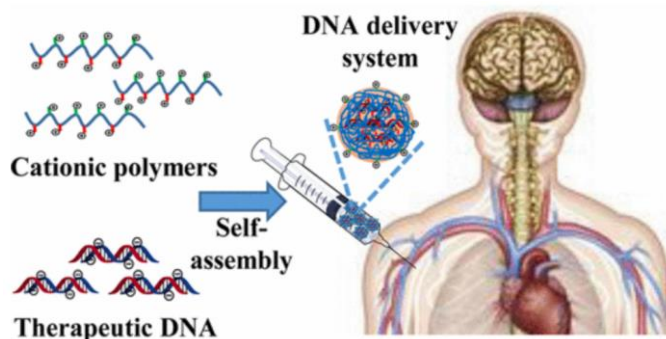
Surface-Adaptive Gold Nanoparticles with Effective Adherence and Enhanced Photothermal Ablation of Methicillin-Resistant Staphylococcus Aureus Biofilm

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Citation: Fu, Y. et al. *Biomacromolecules*, 2017, 18 (8) 2231-2246

Challenges in DNA Delivery and Recent Advances in Multifunctional Polymeric DNA Delivery Systems

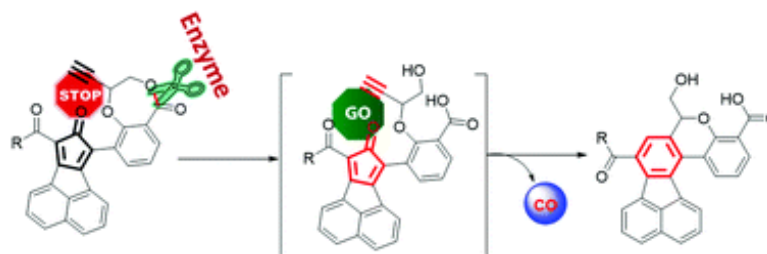


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Citation: Ji, X.; et al. *Chem Commun.* 2017, 53, 8296.

An esterase-activated click and release approach to metal-free CO-prodrugs



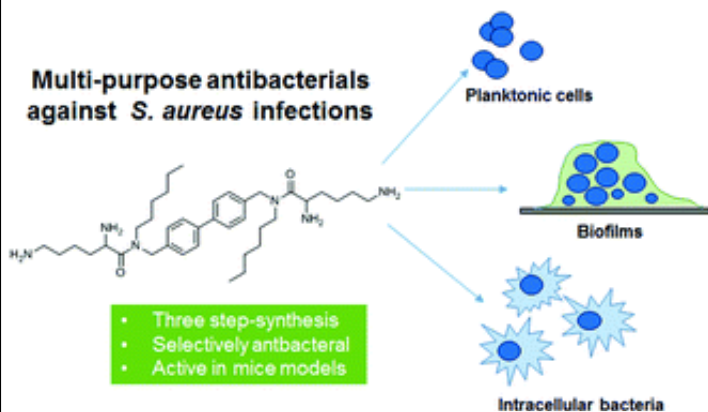
One major challenge in the development of CO as a therapeutic agent is its controllable delivery in a pharmaceutically acceptable form. The authors describe for the first time a general chemical strategy to esterase-sensitive organic CO-prodrugs.

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other

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Citation: Ghosh, C.; *et al. Chem Commun.* **2017**, 53, 7788.

L-Lysine based lipidated biphenyls as agents with anti-biofilm and anti-inflammatory properties that also inhibit intracellular bacteria



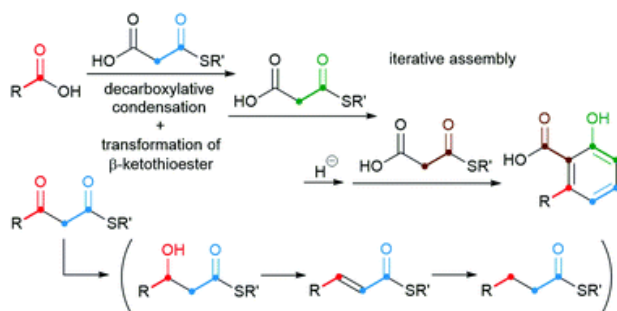
L-Lysines were conjugated to lipidated biphenyls to obtain selective membrane-active antibacterial agents that inhibit cell-wall biosynthesis. The most selective compound bore promising activity against biofilm-related infections and intracellular bacteria, and also suppressed the stimulation of TNF- α induced by lipoteichoic acid. It was also active in a murine model of MRSA infection.

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Citation: Akagawa, K.; Kudo, K. *Chem Commun.* **2017**, 53, 8645.

Biomimetic iterative method for polyketide synthesis



An iterative method for synthesizing polyketides was demonstrated, in which the chain elongation of a carboxylic acid was performed by decarboxylative dehydration condensation with a malonic acid half thioester. After transforming the resulting β -ketothioester into an appropriate form, the carboxylic acid functionality was regenerated for the next elongation step.

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Citation: *JAMA.* 2017;318(4):322. doi:10.1001/jama.2017.8753

Chikungunya Vaccine Trials Begin

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Citation: Peng, et al. *Mor. Pharm.* **2017**, *14*, 2475-2486

Polymeric Nanocarriers Based on Cyclodextrins for Drug Delivery: Host-Guest Interaction as Stimuli Responsive Linker

Stimuli responsive polymers have been extensively studied as nanocarriers for drug delivery systems (DDSs), especially those based on supramolecular interactions. Cyclodextrin (CD) is one kind of widely applied host molecule, and the host-guest interactions between CD and different counterparts can respond to different stimuli and thus can be applied as responsive linkers for polymeric DDSs. In this review, the polymeric nanocarriers based on the host-guest interactions between CD and ferrocene, azobenzene, and benzimidazole as DDSs are summarized, with redox, light, and pH sensitivity, respectively. The mechanisms for the stimuli responsive ability of the linkers, the application of them for construction of DDSs with different polymer structures, and the controlled release behaviors have been focused. In addition, the outlook and challenge of these systems are discussed.

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Citation: Biswas, et al. *Mor. Pharm.* **2017**, *14*, 2518-2528

Intracellular Delivery of Colloidally Stable Core-Cross-Linked Triblock Copolymer Micelles with Glutathione-Responsive Enhanced Drug Release for Cancer Therapy

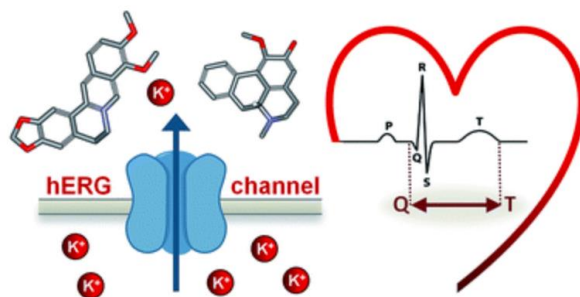
A novel ABA-type triblock copolymer consisting of a hydrophilic central poly(ethylene glycol) block and two terminal hydrophobic blocks of a polymethacrylate having pendant disulfides (PHMssEt), thus PHMssEt-b-PEG-b-PHMssEt (ssTP). Aqueous self-assembly and the following disulfide-exchange reaction of the resulting ssTP allow for formation of core-cross-linked micelles (CCMs) through the formation of new disulfide linkages, retaining enhanced colloidal stability in physiological conditions and in the presence of proteins. Further, they exhibit reduction-responsive enhanced release of encapsulated drugs in response to cellular concentrations of glutathione in cancer cells, confirmed by dynamic light scattering and spectroscopic analysis. Combined with these results, in vitro (cells) and in vivo (mouse model) biological results suggest that ssTP-based CCMs are effective candidates as intracellular nanocarriers targeting tumors for cancer therapy.

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Citation: Kratz, J. M. et al. *Nat. Prod. Rep.*, **2017**, *35*, 957-980

Natural products modulating the hERG channel: heartaches and hope



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Citation: *Nature* **548**, 162–164 (10 August 2017) doi:10.1038/548162a

Therapeutics: Click and discover

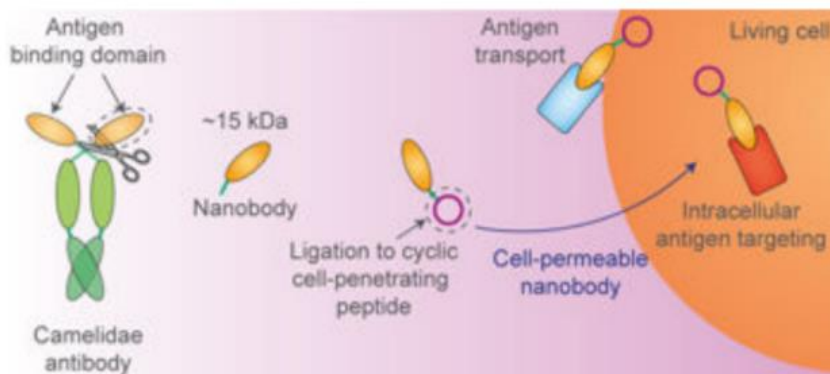
Click chemistry enables preclinical evaluation of targeted epigenetic therapies

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synthesis
mechanism
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other

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Citation: *Nature Chemistry* **9**, 751–761 (2017) doi:10.1038/nchem.2779

Cell-permeable nanobodies for targeted immunolabelling and antigen manipulation in living cells

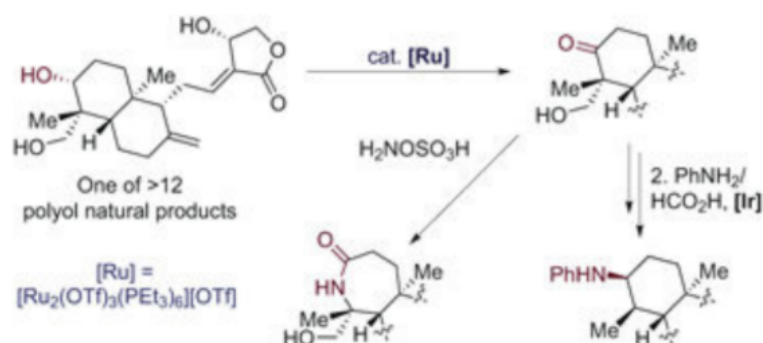


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Citation: *Nature Chemistry* (2017) doi:10.1038/nchem.2835

Site-selective oxidation, amination and epimerization reactions of complex polyols enabled by transfer hydrogenation



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Citation: Hammer, S.K.; Avalos, J.L. et al. *Nat. Chem. Biol.* **2017**, *13*, 823-832

Harnessing yeast organelles for metabolic engineering

Each subcellular compartment in yeast offers a unique physiochemical environment and metabolite, enzyme, and cofactor composition. While yeast metabolic engineering has focused on assembling pathways in the cell cytosol, there is growing interest in embracing subcellular compartmentalization. Beyond harnessing distinct organelle properties, physical separation of organelles from the cytosol has the potential to eliminate metabolic crosstalk and enhance compartmentalized pathway efficiency. In this Perspective we review the state of the art in yeast subcellular engineering, highlighting the benefits of targeting biosynthetic pathways to subcellular compartments, including mitochondria, peroxisomes, the ER and/or Golgi, vacuoles, and the cell wall, in different yeast species. We compare the performances of strains developed with subcellular engineering to those of native producers or yeast strains previously engineered with cytosolic pathways. We also identify important challenges that lie ahead, which need to be addressed for organelle engineering to become as mainstream as cytosolic engineering in academia and industry.

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mechanism
review
other

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Citation: van der Velden, et al. *Nat. Chem. Biol.* **2017**, *13*, 833-835

Autocatalytic backbone N-methylation in a family of ribosomal peptide natural products

nonribosomal peptide synthetases (NRPSs) create structurally diverse peptides through direct incorporation of nonproteinogenic amino acids. This feat is achieved in an assembly-line-like fashion in which individual modules within giant multimodular NRPS proteins are responsible for the activation, incorporation and optional further modification of amino acids.

Nonetheless, while methylation of peptide N termini and side chains have been observed in RiPPs2, backbone N-methylation has only been found in NRPS-derived peptides, where this modification is introduced before amide bond formation and can improve therapeutic peptide metabolic stability, membrane permeability, target selectivity, affinity and oral bioavailability. Despite these favorable properties, backbone N-methylation has, to our knowledge, not been reported as a PTM in any naturally occurring ribosomal peptide or protein.

We show that iterative autocatalytic activity of an N-methyltransferase fused to its peptide substrate is the signature of a new family of ribosomally encoded metabolites.

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synthesis
mechanism
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other

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Citation: Clevenger, et al. *Nat. Chem. Bio.* **2017**, *13*, 895-901

A scalable platform to identify fungal secondary metabolites and their gene clusters

It is estimated that there are between 500,000 and 3 million ascomycete fungal species on earth, each containing on the order of 50-90 BGCs encoding the production of secondary metabolites. However, it has proved challenging to translate this vast biosynthetic potential of fungal genomes into defined and renewable chemical libraries.

The authors established a scalable process for the expression of large numbers of full-length gene clusters, called FAC-MS. Using fungal artificial chromosomes (FACs) and metabolomic scoring (MS), we screened 56 secondary metabolite BGCs from diverse fungal species for expression in *Aspergillus nidulans*. We discovered 15 new metabolites and assigned them with confidence to their BGCs. Using the FAC-MS platform, we extensively characterized a new macrolactone, valactamide A, and its hybrid nonribosomal peptide synthetase-polyketide synthase (NRPS-CPKS). The ability to regularize access to fungal secondary metabolites at an unprecedented scale stands to revitalize drug discovery platforms with renewable sources of natural products.

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synthesis
mechanism
review
other

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DDO
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<p>The Enduring Challenge of Advanced HIV Infection</p>	<p>bioorganic methods synthesis mechanism review other</p>
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<p>We still need to beat HIV</p> <p>Despite remarkable advances in HIV treatment and prevention, the limited political will and leadership in many countries; particularly in West and Central Africa and Eastern Europe; have fallen short of translating these gains into action. As a result, nearly 2 million infections occurred in 2016, creating a situation that is challenging to counter. Antiretroviral therapy (ART) has been the catalyst for change in how HIV infection is treated and prevented. A single, once-a-day, multidrug tablet, with few side effects, has converted HIV from a death sentence to a chronic, manageable disease for millions. It reduces viral levels so that the risk of transmission plummets. Yet, ART is a lifelong and costly regime, and many people in the developed and the developing world cannot access it. Many nations do not have the health care infrastructure or the community engagement to support the robust new ways to prevent transmission or diagnose infection. Although we have come far, the benefits of these new approaches are not universal. The Paris Statement describes five scientific priority areas for building a new public health agenda that meets the challenge of this ongoing epidemic in the face of shrinking resources. HIV persistence and viral control mechanisms must be understood through basic research to envision a functional or complete cure.</p>	<p>bioorganic methods synthesis mechanism review other</p>
	<p>OM Bryo DDO Hybrid Drug Deliv. Prostratin</p>

<p>Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade</p> <p>The preclinical and clinical data that emerged using antibodies against two immune checkpoint proteins, cytotoxic T lymphocyte-associated protein 4 (CTLA4) and programmed cell death receptor-1 (PD-1), led to a paradigm shift in oncology as the treatment of some patients with these drugs led to tumor regression and durable survival for more than a decade (3). But as more patients with various types of cancer have been treated with immune checkpoint therapies, an enduring problem is to identify which patients are likely to respond. Le et al. (4) report the response to anti-PD-1 therapy (pembrolizumab) in 12 different tumor types, and show that patients who responded to the agent had defects in a DNA damage response pathway called mismatch repair.</p>	<p>bioorganic methods synthesis mechanism review other</p>
	<p>OM Bryo DDO Hybrid Drug Deliv. Prostratin</p>

Citation: Servick, K. *Science*. **2017**, *357*, 436-437.

Embryo editing takes another step to clinic

This week, a U.S.-based team published the first rigorous demonstration that the gene-editing method CRISPR can efficiently repair a gene defect in human embryos. Although none of the labmade embryos were transferred into women, the research team, led by embryologist Shoukhrat Mitalipov of Oregon Health and Science University in Portland, says the success paves the way for using the technique in the clinic to prevent the transmission of genetic disease. But evidence of the technique's long-term safety is still lacking, and many researchers and ethicists have argued that germline editing¹—making permanent, heritable changes to the genome that could correct genetic disease, but also theoretically introduce other designer traits²—should for now be limited to research exploring basic biology.

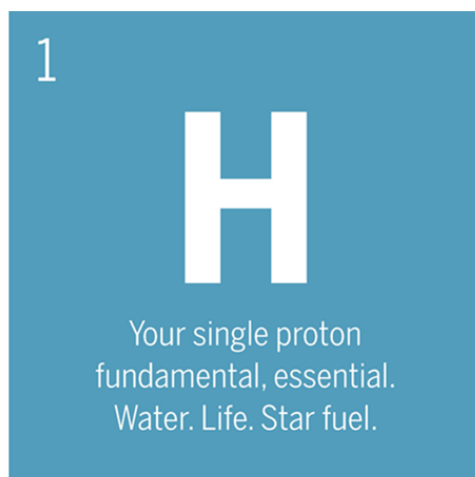
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Citation: Lee, M.S. *Science*. **2017**, *357*, 461-463

Elemental haiku

Author Mary Soon Lee (marysoonlee@gmail.com) provides this review of the periodic table composed of 119 science haiku, one for each element plus a closing haiku for element 119 (not yet synthesized). The haiku encompass astronomy, biology, chemistry, history, physics, and a bit of whimsical flair. For an interactive periodic table displaying each haiku, go to <http://vis.sciencemag.org/chemhaiku>.



bioorganic
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mechanism
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other

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Drug Deliv.
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Citation: Airan, R. *Science*. **2017**, *357*, 465

Neuromodulation with nanoparticles

Current strategies for clinical neuromodulation are limited by either high invasiveness, low precision, or poor depth of penetration. Deep brain stimulation (DBS) and other electrical strategies for deep brain neuromodulation necessitate the use of invasive device placement. Similarly, optogenetic interventions generally require the placement of a fiber-optic cable into the tissue for light delivery and would necessitate gene therapy. Noninvasive techniques for electrical neuromodulation, such as transcranial magnetic stimulation (TMS) or transcranial direct current stimulation (tDCS), on the other hand, have an overly broad spatial extent and limited depth of penetration. Focused ultrasound (FUS) is a near-ideal modality for clinical noninvasive neuromodulation, because it can efficiently deliver energy at significant depth throughout the body. FUS can create millimeter-sized sonication foci in magnetic resonance imaging (MRI)-defined brain regions, across intact skin and skull, while the patient is awake and participating in a neuropsychiatric exam.

For his thesis, he developed the optoXRs, a family of opsin-receptor chimeras that control G protein-coupled signaling pathways using light (3). Using optoXRs, we were able to control not just neuronal firing and intracellular calcium fluxes in the mouse brain but also conditioned place preference, a behavioral model of reward and addiction.



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mechanism
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other

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Citation: Chen, *et al. Science*. 2017, 357, 475-479

Assembly principles and structure of a 6.5-MDa bacterial microcompartment shell

a mechanochemically responsive nonconjugated polymer that converts to a conjugated polymer via an extensive rearrangement of the macromolecular structure in response to force. Our design is based on the facile mechanochemical unzipping of polyadderene, a polymer inspired by a lipid natural product structure and prepared via direct metathesis polymerization. The resultant polyacetylene block copolymers exhibit long conjugation length and uniform trans-configuration and self-assemble into semiconducting nanowires. Calculations support a tandem unzipping mechanism of the ladderene units.

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other

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Drug Deliv.
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