EDITED BY KRISTEN MUELLER AND JAKE YESTON

BIOCHEMISTRY

Targeting Tryptophan

S-adenosylmethionine (SAM) seems like an innocuous combination of an amino acid and a nucleoside, yet it supports a wide variety of biochemical transformations whose scope remains underappreciated. Zhang *et al.* explore its intriguing role in the biosynthesis pathway of the antibiotic nosiheptide—a macrocyclic thiopeptide with an embedded indole. The first step is reductive cleavage of SAM to yield the 5′-deoxyadenosyl radical (5′-dA*) along with methionine. Surprisingly, 5′-dA* goes on in this case to abstract a hydrogen atom, not from the usual suspect (a carbon atom of the substrate), but from the indole nitrogen of tryptophan. This leads to a rather complicated sequence of events, with the final outcome being the release of the nitrogen atom and α-carbon (from the backbone portion of tryptophan) as ammonia and formaldehyde and the attachment of the carboxylate to the indole ring at C2; the indolic acid is then used to make nosiheptide. Having established this mechanism, the authors go on to introduce a fluorinated tryptophan derivative into the medium and show that the fluorinated indole functionality is incorporated (albeit somewhat less efficiently) into the corresponding final product, thereby broadening the structural diversity of this antibiotic class. — GJC

Nat. Chem. Biol. **7**, 154 (2011).

DEVELOPMENT

Hox9 Sets the Stage

An intricate interplay of signaling pathways, which include polarized gradients of Hand2 and Gli3 expression and subsequent Sonic hedgehog signaling, is important early on in anterior-posterior patterning in limb development. How these signaling gradients are established, however, is unknown. Xu and Wellik use mouse genetics to examine whether Hox9 genes, which are expressed along the forelimb anterior-posterior axis, play a role in early mouse limb development. No obvious defects are seen in mice with single mutations of the Hox9 genes (Hoxa9, Hoxb9, Hoxc9, and Hoxd9); however, mutation of all four Hox9 genes resulted in severe forelimb defects, with total loss of the posterior skeletal elements. This phenotype resembles the forelimb phenotype of Shh and Hand2 mutants. Subsequent analysis of in situ mRNA expression revealed that the Hox9 genes act upstream of Hand2 to initiate the posterior limb compartment and Hand2 polarity, which in turn initiates Shh signaling. No defects in hindlimb development were observed in Hox9 mutant mice, which suggested that the role of Hox9 genes in setting up limb polarity is restricted to forelimb development only. — BAP

Proc. Natl. Acad. Sci. U.S.A. **108**, 10.1073/pnas.1018161108 (2011).

ECOLOGY

See You Next Summer

Socially complex species such as humans, elephants, wolves, and orcas establish strong bonds among individuals that persist after periods of separation. These "fission-fusion" dynamics require an ability to recognize individuals even after periods of absence. Such long-term individual recognition has often been attributed to large-brained species with strong sociocognitive abilities; however, bats also display this ability. Whether these dynamics involve individual recognition or are purely driven by behavioral aggregation, however, is unknown. Bechstein's bats (*Myotis bechsteinii*) form stable colonies of females from April through September, which disintegrate during winter. Kerth *et al.* followed the movements of individually marked Bechstein's bats in two well-studied populations over 5 years. Analysis of 20,500 roosting sites revealed that individuals show consistent preference for individual roosting partners, who may differ in age, morphology, and family, and that these preferences persist over years, even after separation. These communities resemble those found in other socially complex species, which suggests that although social complexity is demanding sociocognitively, it may not require a large brain. — SNV

Proc. R. Soc. London Ser. **278**, 10.1098/rspb.2010.2718 (2011).

CHEMISTRY

Ring of Rings

The abstract prospect of using a circle to derive a square has intrigued scholars of geometry for centuries. Segawa *et al.* have now used a square to derive a circle. The arena in this case was chemistry, rather than mathematics, and the task at hand was to assemble a molecular ring composed in turn of 12 benzene rings, linked to one another at the diametrically opposed 1 and 4 positions. Previous efforts had yielded small quantities of this [12]cycloparaphenylene in a mixture of variously sized relatives bearing 9 through 18 benzenes. The key to a more efficient route was a building block linking two benzene rings at an approximate right angle through an intervening cyclohexane diol derivative. By thoroughly optimizing a catalytic nickel system, the authors succeeded in linking four such building blocks in a single reaction medium to form a square with the cyclohexane

CREDITS (TOP TO BOTTOM): ACRO IMAGES GMBH/ALAMY (INSET) GERALD KERTH; XU AND WELLIK, *PROC. NATL. ACAD. SCI. U.S.A.* **108**, 10.1073/PNAS.1018161108 (2011)

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rings at the corners and two benzenes along each edge. Dehydration/aromatization of the corner rings then honed the square into the circular targeted product in sufficient yield to afford a crystal structure. — JSY

Angew. Chem. Int. Ed. **50**, 10.1002/anie.201007232 (2011).

MICROBIOLOGY

Cystic Fibrosis Double Whammy

People with cystic fibrosis (CF) suffer from life-threatening antibiotic-resistant *Pseudomonas aeruginosa* respiratory infections, with consequent chronic inflammation, which generates oxidative stress. *P. aeruginosa* expresses several multidrug efflux systems, including the MexXY-OprM pump, which drives antimicrobial resistance in CF lungs. Expression of MexXY-OprM is unexpected, because ribosome disruption, but not antibiotics such as aminoglycosides, induces its expression, yet CF isolates exhibit high degrees of resistance to aminoglycosides. It turns out that *mexXY* up-regulation depends on the gene PA5471, which is induced by oxidative stress. Fraud and Poole now demonstrate that exposure to inflammation-induced oxidative stress for several days produced a fourfold elevation in aminoglycoside resistance in *P. aeruginosa,* which was indeed mediated by PA5471. Aminoglycoside resistance did not always follow increased *mexXY* expression alone, which suggests that additional genes required for translation or protein synthesis may be involved. Thus, chronic inflammation, rather than antibiotics, drives the expression of MexXY-OprM, which leads to drug resistance in CF lungs. — CA

Antimicrob. Agents Chemother. **55**, 1068 (2011).

CHEMISTRY

Practically Perfect Pi Chains

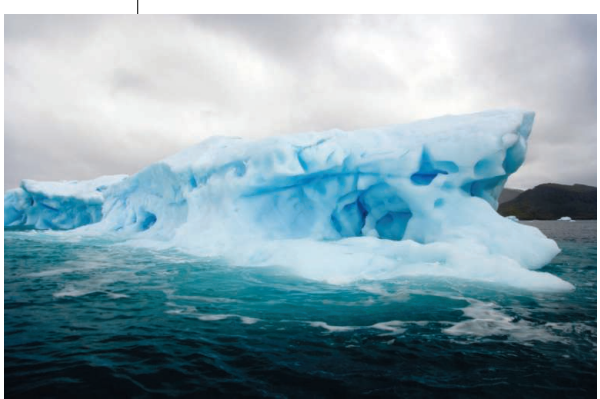
In principle, a planar π-bond network in a conjugated polymer chain should provide a perfect highway for delocalized charge carriers created by photoexcitation. In practice, what should be a rigid molecule has bends and defects that usually cause the polymer chain to segment into localized chromophores. Da Como *et al*. performed broad-band single-molecule photoluminescence (PL) and PL excitation (PLE) spectroscopy on β-phase poly(9,9-dioctylfluorene) oligomers (nine repeat units) and polymers (about 500 repeat units), in which all of the repeat units lie in one plane. Previous studies revealed a narrow emission transition, suggesting single-chromophore behavior, but the emission was not completely polarized, implying that bending defects were present. The authors isolated the molecules at low concentration and obtained spectra at 4 K, and under these conditions, the spectra of the oligomer and polymer were virtually the same—a single 0-0 transition peak at 445 nm, with mirror symmetry between excitation and emission and some excitation of vibrational modes. Thus, only a single exciton is created in the polymer, and it can travel more than 50 times its length along the chain. — PDS

J. Am. Chem. Soc. **133**, 10.1021/ja109342t (2011).

CLIMATE SCIENCE

More and More Melting

One of the most important consequences of global warming is the loss of mass from the Antarctic and Greenland ice sheets, and the rise in sea level accompanying that loss. Measuring changes in the mass of an ice sheet is extremely difficult, due both to the technical challenges involved in collecting good data and the intrinsic variability of the process, but the precision of the applied methods has increased sufficiently over the past decades that even monthly trends can now be discerned. Rignot *et al.* provide an update on the state of mass change of the Greenland and Antarctic ice sheets, using two independent methods in order to demonstrate consistency in the measurements. They find that the rate of ice sheet loss has accelerated over the past 18 years by a combined total of 36.3 ± 2 Gt/year^2, three times faster than that of mountain glaciers and ice caps. If this trend continues, ice sheets will be the largest single contributor to sea-level rise by the end of the 21st century and will probably contribute more to sea-level rise than is currently projected. — HJS



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Geophys. Res. Lett. **38**, L05503 (2011).

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