BIOMEDICINE

The Benefits of Sequestration

About 170 million people worldwide are infected with hepatitis virus (HCV), which causes progressive liver disease, and current antiviral therapies are only partially effective and/or cause adverse side effects. HCV survival and replication require binding of the viral genomic RNA to a noncoding RNA of host origin that is abundant in the liver, called miR-122. Therapies that lower miR-122 levels have been tested in preclinical models of HCV infection with encouraging results.

Janssen *et al*. now report the results of a phase 2a clinical trial designed to assess the safety and efficacy of a chemically modified antisense oligonucleotide that sequesters miR-122 into a stable heteroduplex, thereby inhibiting its function. In a study of 27 HCV-infected patients receiving five weekly injections of the oligonucleotide, those receiving the highest dose showed a substantial decline in plasma HCV levels that persisted for about 15 weeks before rebounding. No significant side effects were observed and, as a bonus, a 25% reduction in plasma cholesterol levels was observed. — PAK

N. Engl. J. Med. **368**, 1685 (2013).

EDUCATION

Motivation + Skill = Success

Both motivational and cognitive variables play a role in academic achievement. The relationship between these variables and academic success at a specific time point has been described, yet there has been little research on whether these variables can predict long-term academic gains. Controlling for intelligence, Murayama *et al*. examined how motivation and strategies used by students to learn the material related to growth in academic achievement in mathematics over time. German students in grades 5 to 10 were assessed longitudinally for both math skills and self-reported motivation and learning strategies, and latent growth curve modeling was used to evaluate growth in mathematics achievement. Results showed that although the initial level of achievement was strongly related to intelligence, motivation and learning strategies predicted growth in math achievement over time. Although correlational, these findings suggest that motivation and learning strategies should be further examined, as one of the ultimate goals in education is to enable sustainable learning. — MM

Child Dev. 10.1111/cdev.12036 (2012).

CREDITS: THINKSTOCK (2)

ANIMAL BEHAVIOR

A Social Shake-up by Song

Song, in birds, is a fundamental means of communication. Research over several decades has revealed how individuals learn, produce, and perceive song, but communication, by definition, occurs among multiple actors. Maguire *et al.* show that changes in song preference in individual female brown-headed cowbirds has cascading behavioral effects, altering social structure and interaction among all the birds within a flock. Targeted lesions that disrupted the song center of the brain in experimental females reduced their preference for the songs of dominant males. When these females were then released back into a mixed social group, their reduced song preference increased their solicitation of males other than their own mates. This in turn inspired other females to also increase solicitation and altered dominance structure among males, who now spent more of their time singing to females. Furthermore, network analysis showed that social networks that included females with lesions were less stable and connected than those containing control females. These results show that behaviors we often think of as specific to an individual, such as dominance, may in fact be emergent properties of group interactions. Simultaneously, they also emphasize the key role that individuals can play in shaping group dynamics. — SNV

PLoS One 10.1371/journal.pone.0063239 (2013).

CHEMISTRY

Brushing Away Toxicity

Osmium tetroxide is among the most useful and versatile oxidizing agents of olefins, accounting for its widespread application in chemistry research despite its dangerous combination of toxicity and volatility. Basavaraju *et al*. have constructed a microfluidic reactor that safely confines the compound without unduly compromising its reaction kinetics. The design incorporates high-surface-area nanobrush polymers that tether the osmium (Os) to the reactor while leaving it readily accessible to the incoming reagents. Coating conventional polydimethylsiloxane with a polyvinylsilazane layer before grafting these brushes rendered the interior of the reactor tolerant to organic solvents. Addition of tetrahydrofuran stabilized the

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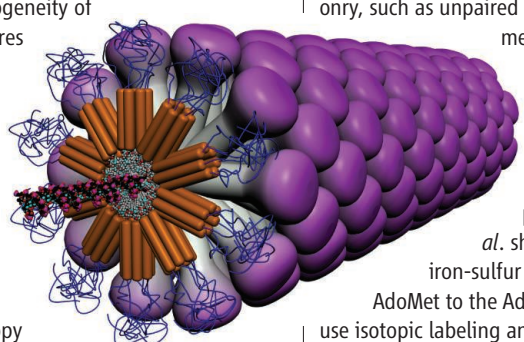
catalytic quantities of the bound Os complex in the +6 oxidation state, after which olefins could be readily dihydroxylated or oxidatively cleaved through reaction with stoichiometric *N*-methylmorpholine-*N*-oxide or periodate, respectively. The system could be reused after 3 months with no degradation in performance. — JSY

Angew. Chem. Int. Ed. **52**, 10.1002/anie.201301124 (2013).

CHEMISTRY

Mimicking Rodlike Viruses

The self-assembly of one-dimensional (1D) structures that have a precise length can be particularly difficult because such assemblies are prone to aggregation, even though these structures are readily formed by rodlike viruses such as the tobacco mosaic virus. Ruff *et al*. have mimicked the assembly of 1D filamentous viruses by encapsulating double-stranded DNA—both linear strands and supercoiled circular plasmids—in water. They used a triblock structure to mimic the protein coat. A cationic spermine unit that binds to DNA is attached to a peptide that forms a compact coiled structure. The other end of the peptide bears a polyethylene glycol (PEG) tail that creates a hydrophilic exterior structure. These mushroom-shaped capsomers bind and encapsulate DNA (for DNA strands 1200 base pairs long, about 1.2 to 1.5 units bind per base pair) and can form structures up to 1.6 μm in length. The homogeneity of the linear structures formed improved with longer PEG tails (5000 versus 2000 monomers), as determined by small-angle x-ray scattering and transmission electron microscopy studies. The larger structures formed by the longer PEG chains appear to stiffen the structure and allow the DNA to work effectively as a linear template, and decrease the fraction of shorter structures that form when DNA buckles and folds back on itself. — PDS



J. Am. Chem. Soc. **135**, 6211 (2013).

BIOMEDICINE

Peptide Prevention

One of the many challenges faced by cancer survivors is the possibility of relapse. Theories as to why cancers relapse after initially responding to therapy are varied and are likely to depend, at least in part, on the type of treatment the patient receives. Engels *et al*. investigated why tumors relapse after successful adoptive T cell therapy in mice. Mice received an injection of a fibrosarcoma cell line that expressed one of a series of defined peptide antigens. Once tumors were established, they were then treated with T cells specific for that antigen. In vitro, T cells killed the tumor cells independent of the peptide's affinity for binding to major histocompatibility complex (MHC), which presents the peptide to T cells. In vivo, however, only mice that received tumors expressing peptides that were able to bind to MHC with high affinity remained cancer-free. Relapse was observed when affinities were less than 10 nM and was associated with less efficient cross-presentation of peptide antigens by stromal cells surrounding the tumor and reduced stromal cell death. Thus, strong interactions between peptide antigens and MHC may prevent relapse by promoting robust T cell responses that target the tumor itself and the surrounding tissue. — KLM

Cancer Cell **23**, 516 (2013).

BIOCHEMISTRY

Attacked by Radicals

Some bonds are easy to break, and enzymes can handle these via general acid-base catalysis; other bonds are tougher nuts to crack, hence enzymes call upon more potent chemical weaponry, such as unpaired electrons. Phosphonate metabolism protein PhnJ is a member of the family of radical *S*-adenosyl-L-methionine (AdoMet) enzymes and breaks the C-P bond in methyl phosphonate. Kamat *et al*. show that the redox active iron-sulfur cluster in PhnJ converts AdoMet to the Ado-CH_2· radical. They use isotopic labeling and mass spectrometry to establish that this radical pulls off the *pro-R* hydrogen from a nearby glycine residue to create a glycyl radical, which turns around and pulls off the hydrogen from a nearby cysteine to create a thiyl radical. It is this third radical that attacks the methyl phosphonate substrate, breaking the C-P bond by homolysis to form a thiophosphate intermediate and freeing the methyl moiety to grab the *pro-S* hydrogen (from the same glycine) as it exits as methane. The thiophosphate collapses intramolecularly to a cyclic phosphate, regenerating the sulfhydryl side chain, which can then go on to catalyze additional rounds of C-P cleavage in concert with the glycyl radical. — GJC

Nature **497**, 132 (2013).

CREDIT: Y. RUFF *ET AL*., *J. AM. CHEM. SOC.* **135**, 16 (2013) © 2013 AMERICAN CHEMICAL SOCIETY