

potential to form memory T cells. Tubo *et al.* used a single-cell adoptive transfer model in mice to answer this question. Nearly all T cell clones produced memory cells, which suggests that breadth is probably an important component of immunological memory. — KLM

*Science*, this issue p. 511

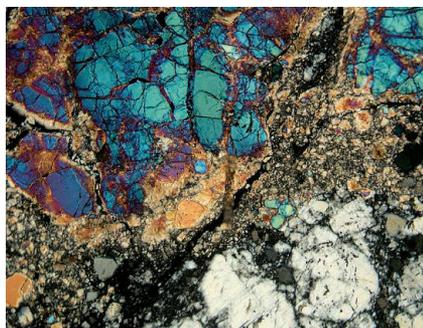
## SEX CHROMOSOME Replacing the Y chromosome

The mammalian Y chromosome encodes a specialized set of genes that are essential for male viability and fertility. In particular, the sex-determining region Y (SRY) protein is necessary to initiate male sex determination. However, Yamauchi *et al.* show that the functions of the entire Y chromosome can be replaced with only two genes. In mice, two transgenes, *Sox9* and *Eif2s3x*, compensated for the absence of all Y chromosome genes to allow successful sperm formation. — BAP

*Science*, this issue p. 514

## LUNAR FORMATION Rehomogenizing the Earth-Moon system

A giant impact formed the Moon, and lunar rocks provide insight into that process. Young *et al.* found that rocks on Earth and the Moon have identical oxygen isotopes. This suggests that well-mixed material from the giant impact must have formed both the Moon and Earth's mantle. The finding also constrains the composition of the "late veneer":



Apollo 17 sample of lunar highland rock

material sprinkled onto Earth after the Moon-forming impact. — BG.

*Science*, this issue p. 493

## METABOLISM Antisense now makes sense

Mipomersen is a U.S. Food and Drug Administration–approved antisense oligonucleotide that lowers low-density lipoprotein (LDL) in patients with high cholesterol by targeting apolipoprotein B (apoB) synthesis. It is unclear exactly how mipomersen works in humans. Reyes-Soffer *et al.* found that in healthy volunteers, the drug reduced levels of LDL and its precursor, very low-density lipoprotein (VLDL), by increasing clearance of both of these vessel-clogging agents rather than reducing their secretion by the liver. Direct clearance of VLDL led to reduced production of LDL. Studies in mice and cell lines revealed how the liver compensates for reduced apoB synthesis to potentially avoid fatty liver disease. — MLF

*Sci. Transl. Med.* **8**, 323ra12 (2016).

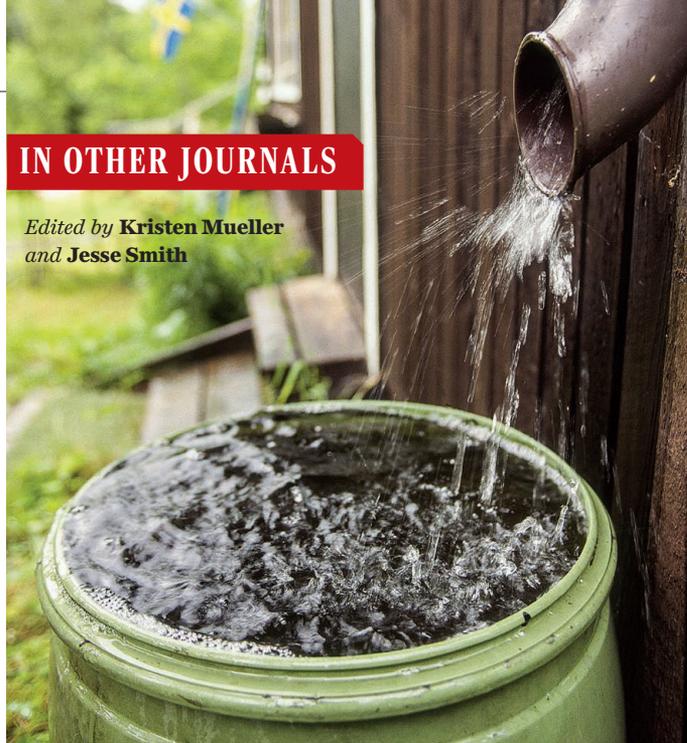
## DEVELOPMENTAL BIOLOGY A MEK threshold in the placenta

The kinases MEK1 and MEK2 have the same substrates, but mice lacking *Mek1* die as embryos because of placental defects, whereas mice lacking *Mek2* are viable. Aoidi *et al.* found that MEK1 and MEK2 were functionally redundant as long as sufficient protein was produced. Producing the minimum amount of MEK in the developing placenta required at least four copies of *Mek2* in mice lacking *Mek1* or two copies of *Mek1* in mice lacking *Mek2*. Thus, the products may be functionally identical, but isoform-specific differences enable isoform-specific regulation and phenotypes. — NRG

*Sci. Signal.* **9**, ra9 (2016).

## IN OTHER JOURNALS

Edited by **Kristen Mueller**  
and **Jesse Smith**



Green potable water systems can harbor elevated levels of pathogens

### GREEN INFRASTRUCTURE

## Saving water—but at what cost?

Strategies to reduce water consumption in buildings may have some unintended consequences. Rainwater cisterns, solar water heaters, and other similar efforts minimize potable water use and reduce energy consumption, but they may also degrade water quality. In a survey of buildings with various green infrastructure, Rhoads *et al.* found that water age, which affects residual chlorine levels, pipe corrosion, and even taste, was significantly greater than that in a conventional home. Consistent with those findings, there were also orders of magnitude more opportunistic pathogens such as *Legionella* species in the green plumbing systems. Reducing water age by eliminating unnecessary storage and regularly flushing pipes may help green water efforts become more widely adopted. — NW

*Environ. Sci. Water Res. Technol.* 10.1039/C5EW00221D (2016).

### EDUCATION

## Flipping for higher exam scores

Active problem-solving in a collaborative environment leads to more effective learning than a traditional lecture. Weaver and Sturtevant report on a 3-year study of a flipped chemistry majors' sequence (lectures are watched outside of class and students participate in group problem-solving and whole-class discussions during scheduled class time). Results collected from standardized

exams showed that the grades of students in the flipped class were significantly higher than those of students in the traditional class. Data collected on the student perspective stressed the importance of carefully planning how the course is taught and carried out, as this will influence the effect it has on students. Overall, this study supports the idea that larger-enrollment courses can be taught using a flipped model. — MM

*J. Chem. Educ.* 10.1021/acs.jchemed.5b00316 (2015).

## PAIN

### A double-drug approach for chronic pain

Chronic pain is a major reason why people visit a doctor. Unfortunately, the underlying causes of chronic pain are still poorly understood. To gain more insight, Ren *et al.* studied a mouse model of neuropathic pain. Nerve injury resulted in a rewiring of neuronal circuits in a region of the brain called the nucleus accumbens, which regulates emotions and addictive behavior. The excitability of some neurons increased, but their number of excitatory synapses fell. Nerve injury also led to reduced extracellular dopamine concentrations in the nucleus accumbens. Combined treatment of mice with dopamine receptor antagonists and a nonsteroidal anti-inflammatory drug blunted neuropathic pain, suggesting potential new drug combinations for treating chronic pain. — PRS

*Nat. Neurosci.* 10.1038/nn.4199 (2015).

## MATERIALS SCIENCE

### Bandages to aid diabetic wound healing

For some conditions, such as diabetic foot ulcers, wound healing can take a long time and may be delayed by the overexpression of proteases such as matrix metalloproteinase-9 (MMP-9). Castleberry *et al.* used layer-by-layer technology to first deposit a water-degradable underlayer onto a nylon bandage, over which they then coated alternating layers of chitosan and small interfering RNA (siRNA). The release profile of the siRNA was controlled by the thickness of the underlayer, whereas the number of siRNA layers could be used to control the overall dose. In mouse models, local delivery of siRNA to an ulcerative wound reduced the production of MMP-9 and thus increased the concentration of extracellular matrix and dramatically improved wound healing. — MSL

*Adv. Mater.* 10.1002/adma.201503565 (2015).

## EPIGENOMICS

### Our varied methylome

Differential methylation of genes has been associated with disease and may play a role in the phenotypic variation between individuals. In order to survey global methylation and to understand how genetic versus nongenetic factors affect methylation, Busche *et al.* used whole-genome bisulfite sequencing on adipose and blood samples from identical and fraternal twins. Although methylation patterns in tissues showed a high degree of similarity between individuals, the authors did find that 15 to 20% of the tissue methylome

varied across individuals, primarily in gene enhancers. More surprisingly, in cases where the environment determined methylation, approximately 60% of the observed variation was unique to the individual. — LMZ  
*Genome Biol.* 16.290 (2015).

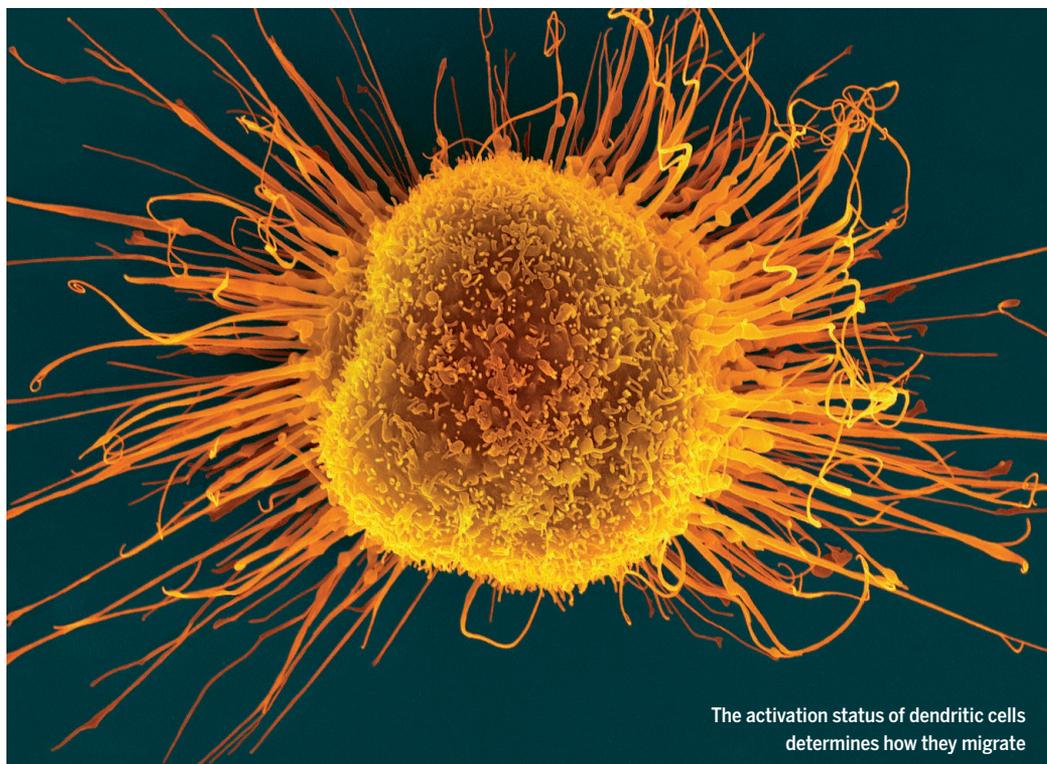
## SYNTHETIC BIOLOGY

### Engineering a bacterial “Deadman” walking

One of the most successful areas of synthetic biology is modifying microorganisms for applications in biotechnology. However, these engineered microbes could pose a risk if released into open

environments. To overcome this, Chan *et al.* engineered two modular gene circuits into the bacteria *Escherichia coli* that act as kill switches. The “Deadman” circuit requires a specific small molecule to prevent a toxin from being expressed and killing the cell. In the “Passcode” circuit, small molecules must induce two transcription factors to inhibit toxin expression. An advantage over other biocontainment systems is that these circuits can be reprogrammed to respond to different inputs or to induce different killing mechanisms. — VV

*Nat. Chem. Biol.* 10.1038/NCHEMBIO.1979 (2015).



The activation status of dendritic cells determines how they migrate

## CELL MIGRATION

### Dendritic cells have two ways to tango

Immature dendritic cells reside in peripheral tissues and use their high migratory capacities to sniff out danger-associated antigens; when they encounter antigens, dendritic cells mature and rapidly migrate to lymph nodes to initiate the adaptive immune response. Vargas *et al.* show that a switch in actin nucleating machineries adapts the dendritic cell migration mode. Arp2/3 nucleates actin at the front of immature dendritic cells, and dendritic cells require it for antigen uptake, but Arp2/3 reduces cell speed and persistence. Mature dendritic cells rely on the formin mDia1 to migrate. mDia1 changes locomotion from diffusive migration to a persistent random walk. This transition helps mature dendritic cells to move along chemokine gradients toward the lymph nodes. — SMH

*Nat. Cell Biol.* 18.43 (2016).