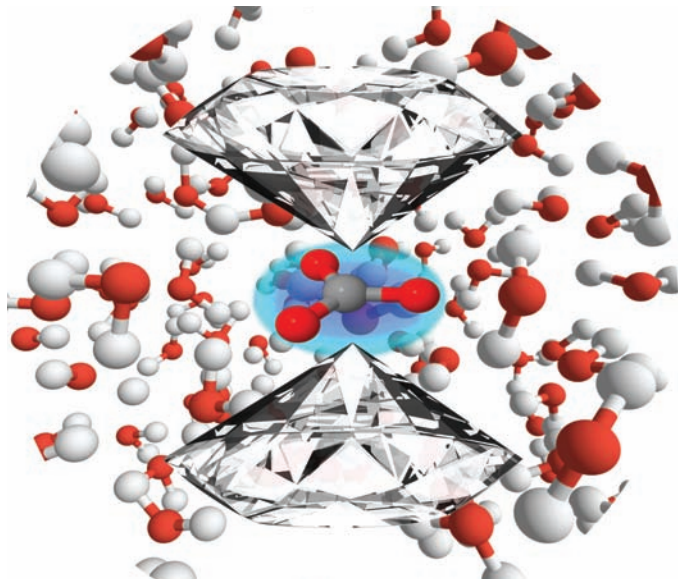




# In This Issue

## Dielectric constant of mantle water helps predict carbonate solubility

Water exhibits substantially different properties at high temperatures and pressures from those observed at ambient conditions on Earth's surface. Researchers have long sought to determine how the extreme temperatures and pressures within Earth's mantle alter the dielectric constant of water, a property that affects mineral solubility and plate tectonics-related processes. But replicating mantle conditions in the laboratory is exceedingly difficult. Using molecular dynamics, Ding Pan et al. (pp. 6646–6650) computed the dielectric constant of water at temperatures and pressures consistent with the Earth's upper mantle and predicted the solubility of carbonates at tectonic plate intersections known as subduction zones. When two tectonic plates collide, the denser plate is thrust downward, or subducted, into the upper mantle, where intense heat and pressure break down rocks and minerals. Based on the calculated dielectric constant, the authors predicted the solubility product of magnesite, an important carbon-bearing mineral in the mantle, suggesting that aqueous mantle fluids may transport carbon deep into the Earth. The study reveals an important property of water that could help improve models of water–rock interactions and advance the study of Earth's carbon cycle, according to the authors. — T.J.



Schematic depicting water and a carbonate ion under high pressure.

## A progesterone-activated ion channel in sperm

The steroid hormone progesterone regulates events such as ovulation, breast development, and suppression of preterm labor. In addition, progesterone within the female reproductive tract activates a calcium ion ( $\text{Ca}^{2+}$ ) channel in human sperm, causing a rapid elevation of intracellular  $\text{Ca}^{2+}$  levels and leading to enhanced motility and stimulation of fertilization. By studying sperm from an infertile

male with a homozygous deletion in a subunit of the CatSper  $\text{Ca}^{2+}$  channel, James Smith et al. (pp. 6823–6828) determined that CatSper is the progesterone-activated  $\text{Ca}^{2+}$  channel in sperm. Only 10% of CatSper-deficient spermatozoa appeared to have normal tails, and of these, only 40% were found to be motile. The authors used a patch-clamping technique on normal-looking spermatozoa from the CatSper-deficient male patient and found no detectable progesterone-activated current. By conducting similar tests on spermatozoa from fertile males, the authors found that sensitivity of CatSper to progesterone arises early in sperm development and increases from testicular to ejaculated stages, although only ejaculated sperm demonstrates desensitization to progesterone following repeated exposures, suggesting that seminal plasma modulates CatSper-dependent signaling. The progesterone binding site of CatSper might represent a target for the development of a male-specific contraceptive, according to the authors. — C.B.

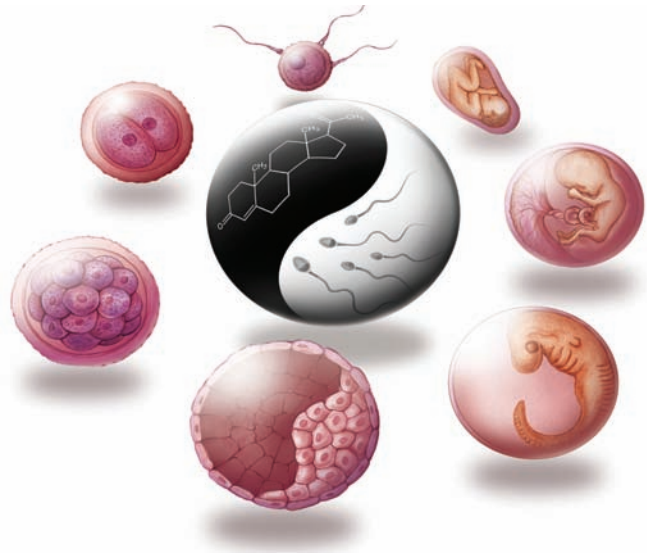


Image courtesy of Carin L. Cain, www.carincain.com.

Progesterone: female hormone for pregnancy and male fertility.

## Divergence of 13- and 17-year life cycles in periodical cicada lineages

Three distinct periodical cicada lineages in the eastern United States have 13- or 17-year life cycles. To determine how the synchronized life cycles evolved, Teiji Sota et al. (pp. 6919–6924) analyzed nuclear and mitochondrial DNA markers for samples collected throughout the eastern United States between 1978 and 2008 from all known periodical cicada species. The authors found that the earliest divergence occurred 3.9 Mya with one branch forming the Decim species group, followed by the subsequent splitting of the other branch 2.5 Mya into the Cassini and Decula species groups. The three lineages independently diverged into 13- and 17-year life cycles, with the earliest split occurring in the Decim lineage 0.5 Mya and all three lineages experiencing at least one instance of life-cycle divergence since the peak of the last glacial period about 19,000–26,500 years ago. The authors suggest that synchronization of life cycles between invading

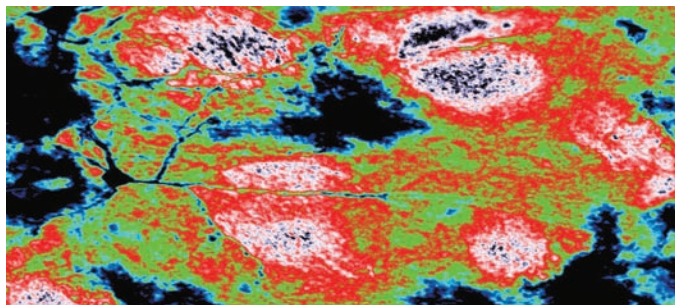
cicada populations and resident populations may have been favored by natural selection possibly because synchronization helped invaders escape predation. According to the authors, the presence of repeated, independent life cycle shifts in all three lineages implies that the species groups may share a common genetic basis for the 13- and 17-year life cycles, which originated prior to the divergence of the species groups. — S.R.



*Magicicada tredecim* of brood XIX emerged in 2011.

## Conversion of fibroblasts into neurons

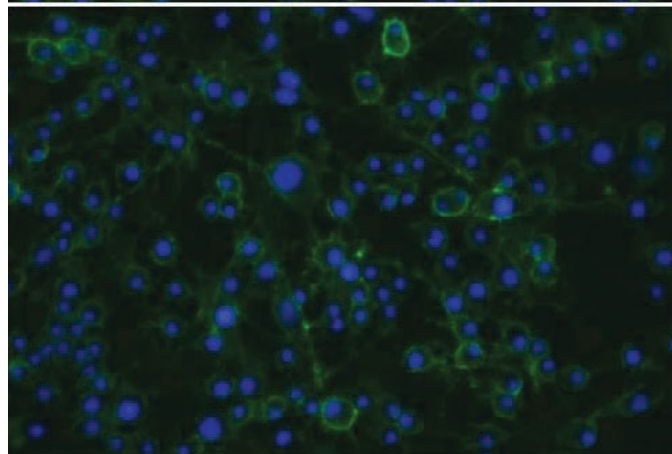
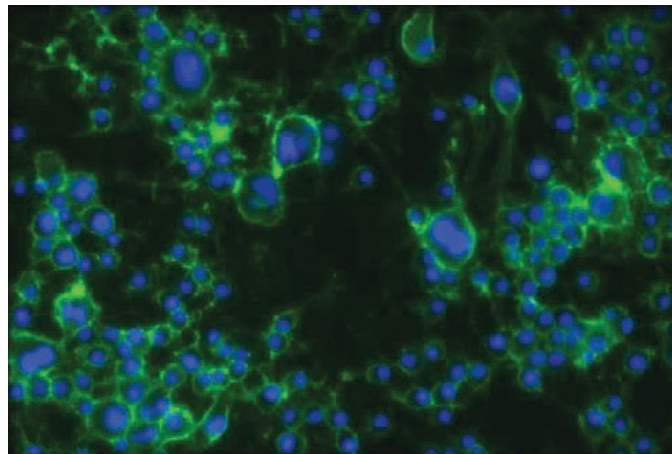
Researchers can generate pluripotent stem cells capable of becoming any human cell type by altering the expression of certain genes in somatic cells. Further, fibroblasts—cells that normally produce connective tissue—can be directly transformed into functioning neurons for use in potential treatments for conditions such as Parkinson disease. Olof Torper et al. (pp. 7038–7043) reveal how human fibroblasts and nervous system cells known as astrocytes can be engineered to turn on a set of neural reprogramming genes and transformed into neurons after being transplanted into the rodent brain. The authors used viral vectors to deliver three reprogramming genes—*Ascl11*, *Brn2a*, and *Myt11*—to human fibroblasts or astrocytes. The genes, collectively known as ABM, were engineered to express in the presence of doxycycline—an antibiotic typically used to achieve regulated gene expression. The authors grafted the cells into the rat brain, administered doxycycline to the rats, and observed the cells' transformation into functional neurons *in vivo*. In a separate experiment, injection of the viral vectors into the mouse brain activated ABM gene expression and coaxed resident glia cells to develop into neurons. The findings illustrate that transplanted human cells and resident mouse cells can be directly converted to neurons in the adult rodent brain via cellular reprogramming, according to the authors. — A.G.



Induced neuron (black) obtained from *in vivo* reprogramming.

## A drug discovery platform for prion diseases

Several prion diseases are known to be infectious, fatal, and incurable. The neurodegenerative disease Creutzfeldt-Jakob disease (CJD), for example, is triggered by the misfolded form of a mammalian protein called PrP, which propagates through self-replication and leads to deposits of pathogenic protein aggregates in the brain. Yervand Karapetyan et al. (pp. 7044–7049) developed a high throughput assay to sift through a collection of drugs approved for human use and identify compounds that reduce the expression of the PrP protein in mammalian cells. Because the physiological function of PrP remains unestablished and the protein is thought to be dispensable, the authors reasoned that drugs that reduce the expression of the protein might serve as potential prophylactic or therapeutic agents against some prion diseases. The authors report that the human seasonal allergy drug astemizole not only reduced the expression of PrP on the surface of lab-grown mouse neuroblastoma cells but also inhibited prion replication in cells infected with either of two distinct prion strains. Further, the authors report that a 30-day treatment regimen using the drug, which can cross the blood-brain barrier, led to a moderate increase in the length of survival of prion-infected mice, compared with untreated mice, suggesting that the drug's potential as a treatment for prion diseases such as CJD merits further exploration. According to the authors, the findings demonstrate the potential of the high-throughput screen as a drug discovery platform. — P.N.



Prion protein (green) at the surface of control neuroblastoma cells (*Top*) or of drug-treated cells (*Bottom*).