

include human pathogens such as human rhinovirus, which causes the common cold, and poliovirus. Most of these viruses are stabilized by a factor that binds in a hydrophobic pocket of the capsid protein VP1, and antiviral compounds can act by displacing this factor. Liu *et al.* report the crystal structure of EV-D68 and its complex with the antiviral compound peconaril. In EV-D68, the hydrophobic pocket contained a fatty acid that was displaced by peconaril. Peconaril efficiently inhibited EV-D68 infection of cells, making it a possible drug candidate against EV-D68. — VV

Science, this issue p. 71

ORGANIC CHEMISTRY

Breaking through the milligram floor

When chemists synthesize compounds, the threshold for success is at least a milligram of product. This has been true for decades—even though biochemical assays have long since descended into microgram territory—and results in part from the constraints of characterization methods. Buitrago Santanilla *et al.* present an automated dosing and characterization protocol for optimizing chemical reaction conditions on the microgram scale. This allowed them to screen numerous base and ligand combinations for catalytic C-N bond-forming reactions between complex pairs

of compounds, in short supply, that resisted standard coupling conditions. — JSY

Science, this issue p. 49

IMMUNOLOGY

An immunological fountain of youth

mTOR signaling, a multipurpose pathway, controls all aspects of cell growth and motility and can also delay onset of aging-related diseases in many species. Mannick *et al.* now show that mTOR inhibition can benefit humans, too. They evaluated whether the mTOR inhibitor RAD001 could reverse the deterioration of immune function seen as people age. By assessing their elderly subjects' reaction to an influenza vaccination, the authors showed that RAD001 boosted their vaccine-induced immune defenses. — OMS

Sci. Transl. Med. **6**, 268ra179 (2014)

CANCER

Overcoming drug resistance in cancer

Cancer patients frequently develop drug resistance. Martz *et al.* devised a method of identifying pathways causing resistance in cancer cells and found that Notch signaling mediated resistance to drugs used in breast cancer and melanoma. Winter *et al.* also used this screening method for myeloproliferative neoplasms, which often have an activating mutation in the kinase JAK2 but are resistant to JAK inhibitors. They pinned the cause of this resistance to RAS, a signaling protein. Thus, screening entire signaling pathways instead of individual genes can identify new therapeutic targets that may be important in multiple types of drug-resistant cancers. — LKF

Sci. Signal. **7**, ra121 and ra122 (2014).

IN OTHER JOURNALS

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

Avoiding nighttime eating may reduce the effects of an unhealthy diet



METABOLISM

You are not just what, but when you eat

Limiting food intake to an 8-hour window that corresponds to a time of high activity protects mice from obesity and metabolic disease caused by a diet high in fat. Chaix *et al.* extended such studies to examine what would happen in a regimen more adaptable to peoples' lifestyles. Promisingly, they found protective effects from fasting periods as short as 12 hours. Even better, mice showed improved metabolic fitness even when they took the weekends off. This was most likely because the changes in gene expression caused by restricting food during the week continued even when mice had full access to food on the weekends. — LBR

Cell Metab. **20**, 991 (2014).

BIOGEOGRAPHY

Origins of the Southern Hemisphere flora

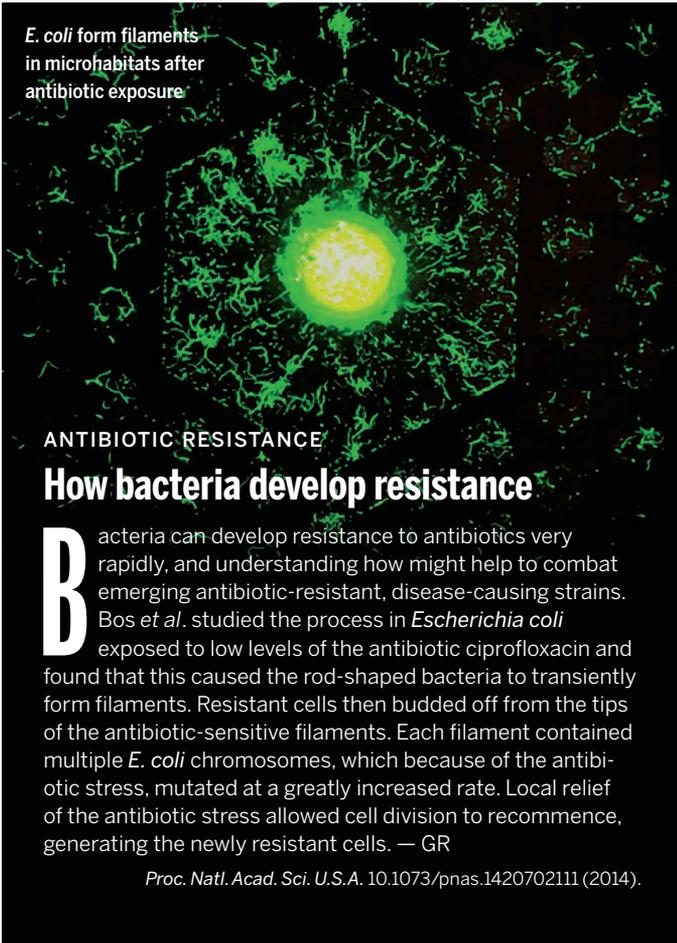
Which plants of the Southern Hemisphere represent descendants of the ancient flora of Gondwana, the southerly part

of the supercontinent Pangaea? Evidence from molecular clocks suggests that many plant lineages descended from a more recent common ancestor. Wilf and Escapa challenge this view by comparing molecular origin dates with fossil dates for groups



PHOTOS: (LEFT TO RIGHT) PHLOX/ISTOCKPHOTO; © D. HURST/ALAMY

E. coli form filaments in microhabitats after antibiotic exposure



ANTIBIOTIC RESISTANCE

How bacteria develop resistance

Bacteria can develop resistance to antibiotics very rapidly, and understanding how might help to combat emerging antibiotic-resistant, disease-causing strains. Bos *et al.* studied the process in *Escherichia coli* exposed to low levels of the antibiotic ciprofloxacin and found that this caused the rod-shaped bacteria to transiently form filaments. Resistant cells then budded off from the tips of the antibiotic-sensitive filaments. Each filament contained multiple *E. coli* chromosomes, which because of the antibiotic stress, mutated at a greatly increased rate. Local relief of the antibiotic stress allowed cell division to recommence, generating the newly resistant cells. — GR

Proc. Natl. Acad. Sci. U.S.A. 10.1073/pnas.1420702111 (2014).

of plants in Patagonia, such as cycads, that are incontrovertibly Gondwanan. They find that the molecular dates are artificially recent even for these ancient groups, and are a poor match for the reliable fossil dates. These findings suggest that biogeographers may have to temper reliance on molecular evidence for determining how flora dispersed. — AMS

New Phytol. 10.1111/nph.13114 (2014).

SURFACE CHEMISTRY

Assessing slow surface heating

Calorimetry can provide essential information about surface reactions, but the small amount of heat released from a surface makes experiments challenging. Pyroelectric detection can measure the heat produced when molecules are adsorbed by a thin metal surface, but calibration is simple only for

rapid reactions (ones over in ~30 ms). For slower reactions, it is more difficult to assess how the experimental setup distorts the signal. Wolcott and Campbell report a fast Fourier transform method that can deconvolute the measured signal for slower reactions. They use it to reproduce successfully how heat is generated when methyl iodide is adsorbed by a platinum surface, as determined with a more complex modeling method. — PDS

Surf. Sci. 10.1016/j.susc.2014.11.005 (2014).

HEART DISEASE

Triglycerides, bedside to bench

Blood tests for heart disease risk measure cholesterol and fat molecules called triglycerides. Interest in triglycerides recently intensified with the discovery that people who carry mutations that disrupt the function

of a glycoprotein called APOC3 (apolipoprotein C-III) have lower plasma triglyceride levels and a reduced risk of heart disease. Scientists thought APOC3 inhibited lipoprotein lipase, an enzyme catalyzing triglyceride breakdown. Gaudet *et al.* now reveal a more complicated mechanism. They found that three patients who had extremely high triglyceride levels because of a genetic deficiency in lipoprotein lipase nonetheless benefited from a drug that inhibits APOC3 synthesis. Clearly, APOC3 still has secrets to reveal. — PAK

N. Engl. J. Med. 371, 2200 (2014).

ULTRAFAST OPTICS

Constraining the speed of tunneling

In contrast to expectation and experience in the classical world, a particle in the quantum world hitting a barrier can appear on the other side, having tunneled through the otherwise impassible obstruction. Debate about how quickly tunneling occurs has existed almost since the discovery of quantum mechanics. Now, Landsman *et al.* use ultrafast optical techniques to measure the amount of time it takes to ionize a helium atom. By following an electron on attosecond time scales as it passes through the energy barrier and leaves the bonds of its parent atom, the authors rule out certain theoretical possibilities, thereby providing a clearer picture of the tunneling process. — ISO

Optica 1, 343 (2014); 10.1364/optica.1.000343 (2014).

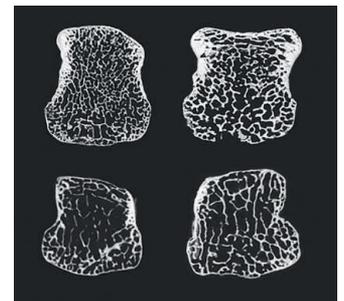
PLANETARY ACCRETION

Tacking the mantle for planet formation

Earth's distance from the Sun and its mass help constrain planetary accretion models. Rubie *et al.* use the initial composition of the mantle as another constraint for accretion simulations, by considering the chemical effects of metallic core formation. The simulations that produce

a realistic Earth require that impacting planetesimals span a range of compositions, metal-silicate element equilibration occurs at progressively greater depths as the planet grows, and only a small amount of interaction takes place between the metal impactor core and the proto-mantle. Adding terrestrial mantle composition to accretion simulations provides insights into the most important factors for planetary formation. — BG

Icarus 10.1016/j.icarus.2014.10.015 (2014).



CT scans of hand bones from (clockwise from top left): chimp, *Australopithecus*, Neandertal, modern human.

PALEOANTHROPOLOGY

Human skeleton became lighter over time

Chimp bones are packed with microscopic structures known as spongy bone; modern human bones aren't, increasing risk of fractures and osteoporosis. Two studies propose an explanation for this change: Chirchir *et al.* found that skeletons from modern chimpanzees, *Australopithecus africanus*, Neandertals, and early *Homo sapiens* all had higher densities of spongy bone than modern humans, suggesting that our sedentary lifestyle is to blame. Ryan and Shaw also found lower spongy bone density in the hip joints of ancient farmers compared with hips from nonhuman primates and ancient hunter-gatherers, supporting the idea that a lack of rigorous exercise, not evolutionary pressure, is responsible for our weak bones. — LW

Proc. Natl. Acad. Sci., 10.1073/pnas.1411696112 (2014), 10.1073/pnas.1418646112 (2014).

Science

How bacteria develop resistance

Guy Riddihough

Science **347** (6217), 39-40.

DOI: 10.1126/science.347.6217.39-c

ARTICLE TOOLS

<http://science.sciencemag.org/content/347/6217/39.3>

RELATED CONTENT

<file:/content/sci/347/6217/twil.full>

PERMISSIONS

<http://www.sciencemag.org/help/reprints-and-permissions>

Use of this article is subject to the [Terms of Service](#)

Science (print ISSN 0036-8075; online ISSN 1095-9203) is published by the American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005. 2017 © The Authors, some rights reserved; exclusive licensee American Association for the Advancement of Science. No claim to original U.S. Government Works. The title *Science* is a registered trademark of AAAS.