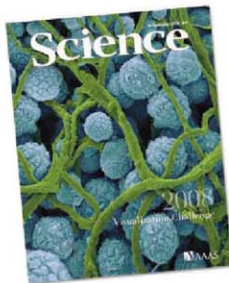


26 September 2008 | \$10

Science

2008
Visualization Challenge

 AAAS



COVER

Boulders and roots, or spores and hyphae? Parallel microscopic and macroscopic worlds merge in this detail from one of the winners of this year's *Science*/NSF International Science & Engineering Visualization Challenge. See the special section beginning on page 1767.

Image: Colleen Champ, with micrographs by Dennis Kunkel

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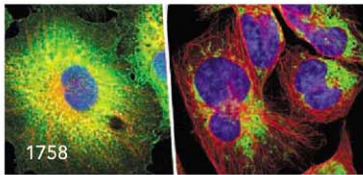
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Transient exposure of mouse fibroblast and liver cells to an adenovirus vector carrying factors that induce pluripotency generates stem cells without viral elements in the genome.

10.1126/science.1162494

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Conservation and Rewiring of Functional Modules Revealed by an Epistasis Map in Fission Yeast
A. Roguev et al.

Comparison of genetic wiring in two types of yeast reveals that protein complexes are conserved, but the interactions between them can change radically between species.

10.1126/science.1162609

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10.1126/science.1162950

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M. Lobino, D. Korystov, C. Kupchak, E. Figueroa, B. C. Sanders, A. I. Lvovsky
A method requiring only the light from a laser as an input yields a full characterization of quantum optical processes by probing its effect on classical states.

10.1126/science.1162086

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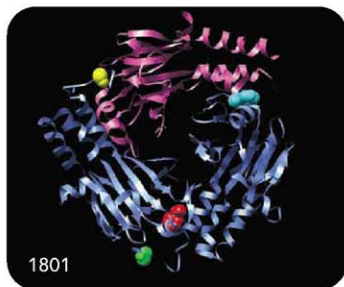
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K. A. Hoffman and B. S. Singer

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An Integrated Genomic Analysis of Human Glioblastoma Multiforme
D. W. Parsons et al.

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Quantum Communication with Zero-Capacity Channels

1812

G. Smith and J. Yard

Two quantum communication channels, each of which is so noisy that it has zero capacity to independently transmit information, can do so when used together.

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A. E. Bragg, M. C. Cavanagh, B. J. Schwartz

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S. Stanley, L. Elkins-Tanton, M. T. Zuber, E. M. Parmentier

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J. O'Neil, R. W. Carlson, D. Francis, R. K. Stevenson

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>> News story p. 1755; Science Podcast

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Infants' Perseverative Search Errors Are Induced by Pragmatic Misinterpretation 1831

J. Topál, G. Gergely, Á. Miklósi, Á. Erdőhegyi, G. Csibra

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B. W. Han, B. R. Herrin, M. D. Cooper, I. A. Wilson

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Disruption of the CTRF Gene Produces a Model of Cystic Fibrosis in Newborn Pigs 1837

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K. Podsypanina et al.

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C. Efferson, R. Lalive, E. Fehr

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M. R. Delgado, A. Schotter, E. Y. Ozbay, E. A. Phelps

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Toad troubles.

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Conservation Efforts May Have Backfired for Spanish Toad

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Wasps Make Peace With Past Enemies

The insects steer clear of foes they have fought in the past.

Fat Molecule Fights Weight Gain

Compound prevents mice from storing unhealthy fat.



Dave Jensen tools up his own career.

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Tooling Up: My Career Dissected

D. Jensen

Dave Jensen highlights some of his own career mistakes.

From Watching 'The Expert' to Being an Expert

L. Cahoon

Melanie Lee attributes her success partly to a childhood TV show.

Union Aftershocks in California

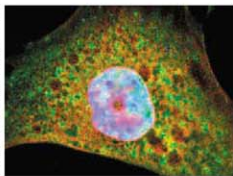
C. Rey

Postdocs and others in the University of California system adjust to life with a union.

The Science Careers Web Log

Science Careers Staff

Here's where to find information from around the Web on careers in the sciences.



Intracellular colocalization of Grb10 and IGF-1 receptors.

SCIENCE SIGNALING

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RESEARCH ARTICLE: Nedd4 Controls Animal Growth by Regulating IGF-1 Signaling

X. R. Cao, N. L. Lill, N. Boase, P. P. Shi, D. R. Croucher, H. Shan, J. Qu, E. M. Sweezer, T. Place, P. A. Kirby, R. J. Daly, S. Kumar, B. Yang
Nedd4 acts through Grb10 to enhance insulin-like growth factor signaling and control animal growth.

PERSPECTIVE: Caspase-2—Vestigial Remnant or Master Regulator?

C. M. Troy and E. M. Ribe

Both mitochondrial-dependent and -independent cell death pathways are mediated by caspase-2.

PODCAST

E. M. Adler, N. R. Gough, A. M. VanHook

Bacteria secrete factors that regulate genes that contribute to virulence.

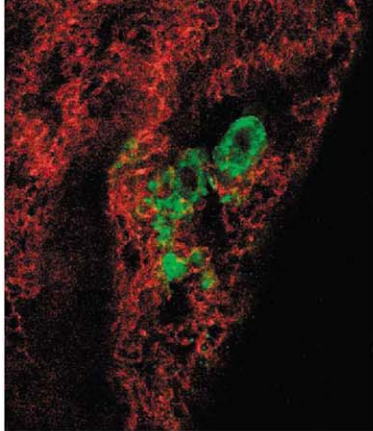
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<< Rethinking Cancer Metastasis

Most human cancer deaths are caused by metastasis, in which cancer cells spread from the primary tumor to new sites in the body. Because metastatic cells must successfully negotiate a series of complex steps, including survival in the bloodstream and establishment in a foreign tissue environment, metastasis has been viewed as a late event in cancer progression. Podsypanina *et al.* (p. 1841, published online 28 August; see the Perspective by Klein) suggest that the metastatic process may begin earlier than previously thought. Normal mouse mammary cells were genetically manipulated to allow the timing of oncogene expression to be experimentally controlled and injected into the bloodstream of mice. Surprisingly, in the absence of oncogene expression, normal mammary cells were capable of traveling to and surviving in the lungs for up to 16 weeks, although they did not initiate aggressive growth until after oncogene activation. Thus, metastases might arise from disseminated normal (pre-malignant) cells that remain clinically silent until genetic changes render them malignant.

DNA Templates for Nanomachinery

The precise and complementary base pair matching in DNA has increasingly led to its use as a building or templating material in the assembly of nanoscale objects like particles or wires, or for the decoration of particles and wires with metals or other molecules. Aldaye *et al.* (p. 1795) review recent developments in the use of DNA as a precise positional tool for complex material assembly. Developments have moved from simple one-dimensional templating to two and three dimensions, with scope for dynamically changing the shape or size of an object, or the fabrication of nanomachines.

Cancer Genomes: From Chaos Comes Order?

Identification of the genes altered in cancer cells is critical for understanding how the disease arises and for designing more effective diagnostic tests and therapies (see 5 September news story by Kaiser).

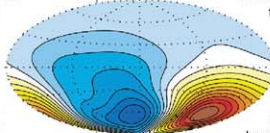
Parsons *et al.* (p. 1807, published online 4 September) and Jones *et al.* (p. 1801, published online 4 September) catalog the numerous genomic alterations that help turn normal cells into two of the deadliest human cancers: glioblastoma multiforme (the most common type of brain cancer) and pancreatic cancer. Although for each cancer type, the specific genomic alterations varied from tumor to tumor, the altered genes affected a limited number of cellular signaling pathways and

regulatory processes, suggesting that these are the pathways that go awry and lead to the disease. Of particular interest in the glioblastoma study was the discovery of recurrent mutations in the active site of isocitrate dehydrogenase 1, encoded by the *IDH1* gene. In this small study, *IDH1* mutations were more prevalent in glioblastomas from younger patients and in "secondary" glioblastomas, and they were associated with a better prognosis.

Martian Dynamo

One surprise from recent spacecraft observations of Mars is that its crust in the southern hemisphere is strongly magnetized, but not so in the northern hemisphere. This pattern seems similar to the major crustal difference on Mars in that the northern hemisphere is relatively smooth, at a much lower elevation, and younger. Mars now lacks an active dynamo.

Stanley *et al.* (p. 1822; see the news story by Kerr and the Perspective by Langlais and Hagay) show through numerical models that if the heat flow were



lower across the core-mantle boundary in the northern hemisphere, as might be expected from any mechanism producing the crustal dichotomy, the resulting geomagnetic field might not be a dipole but be concentrated just in the south. Such a dynamo would also affect Mars' atmospheric evolution because only part of the planet would be strongly shielded from the solar wind.

Working Together to Get the Job Done

Bob tries to make a call to Alice but finds that the line is too noisy. Picking up his second phone (he's a very busy builder), he finds that line is also too noisy and so gives up trying to contact her. With two bad lines, Bob wouldn't be able to make that phone call, at least using the classical communication channels of his provider. Had he had access to quantum communication channels, Smith and Yard (p. 1812, published online 21 August; see the Perspective by Oppenheim) show theoretically that the situation is quite different. Two quantum channels, each with zero capacity to transmit information independently, will allow information to be carried across them when used together. Not only of theoretical interest, this counterintuitive result may be of practical use in the design of quantum communication networks.

Dissecting a Disordered Material

Graphite oxide was first prepared almost 150 years ago, but the functionalization of the graphite is not uniform, which has hampered efforts to characterize it. This material is now of interest as a precursor for the formation of graphene, which has potentially useful electronic properties. Cai *et al.* (p. 1815) have now prepared graphite oxide from graphite with varying degrees of ^{13}C -labeling (up to almost 100%). The labeled product allowed much higher resolution in solid-state nuclear magnetic resonance studies and excluded some of the potential models for the chemical bonding network of this material.

Continued on page 1739

Sodium's Nonlinear Response

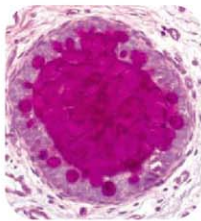
The influence of solvent rearrangements on chemical reactions in solution is often modeled using the linear response approximation, which essentially dictates that all starting configurations that equilibrate to a given final state do so with the same dynamics. **Bragg et al.** (p. 1817; see the Perspective by **Stratt**) show that the approximation comes up short for the formation of neutral sodium-electron ion pairs in tetrahydrofuran. Equilibration is twice as fast when the reaction proceeds by reduction of a Na^+ precursor than when Na^+ is oxidized. The breakdown can be attributed to the large size differences between the cation, anion, and neutral, which substantially alter the extent of necessary solvent cavity rearrangements in each case.

Modeling Ocean Circulation

Hydrothermal systems along ocean ridges help control the chemistry of the oceans and alter and hydrate the upper oceanic crust; this, in turn, returns water to the Earth's mantle at subduction zones. Hydrothermal systems also foster deep ocean ecosystems. Observations seem to indicate that although ocean ridges are broadly linear, outflows are spaced out along them. **Comou et al.** (p. 1825) have developed a three-dimensional numerical model of this flow to help reveal the dynamics. Their model shows that optimizing heat transfer causes the flows to self-organize into narrow pipe-like upflows, spaced about 500 m apart, led by zones of warm downflow that recirculate up to a quarter of the heat.

Cystic Fibrosis Remodeled

Cystic fibrosis (CF) is caused by mutational disruption of *CFTR*, a gene encoding an ion channel required for chloride- and bicarbonate-mediated fluid secretion in epithelia and for salt absorption in many organs. Two decades of intense research on *CFTR* has not yet translated into new clinical therapies, in part because mice—the traditional animal model for human disease research—do not develop the full spectrum of pathologies seen in human CF. To address this problem, **Rogers et al.** (p. 1837) have inactivated the *CFTR* gene in pigs, an animal that shares many anatomical and physiological features of humans. Newborn pigs lacking *CFTR* developed many of the gastrointestinal pathologies seen in infants with CF, including intestinal obstruction and abnormalities of the pancreas, liver, and gallbladder, and their nasal epithelia showed defects in chloride transport. These results, while still preliminary, suggest that the pig model may be a valuable tool for testing new therapies for CF.



From the Minds of Babies

Human babies between 8 months and a year of age cannot perform certain cognitive tasks. In one of these, called the A-not-B error, an object is hidden under a container and the infant repeatedly reaches for it. Then the experimenter hides the object under a different container, in full view of the infant, but the baby still looks under the first container to find it. **Topál et al.** (p. 1831) propose a new explanation for this error, suggesting that the socially intense "teaching" interaction that usually accompanies the repeated hiding of the object under the first container ensures strong association of the object with that location. When the object is hidden without any communication between the experimenter and the infant, the baby's error rate is reduced. Previous explanations for the phenomenon suggested that it was due to the immaturity of the infant's executive motor control or his or her limited cognitive capacities.

The Agony of Defeat

Auctioneers take advantage of human nature to increase the sale prices of items. But are they banking on the successful bidder's enjoyment of winning, or are they instead relying on the bidder's aversion to losing? Two sides of the same coin, one might say, but **Delgado et al.** (p. 1849; see the Perspective by **Maskin**) argue that it is the latter that drives the phenomenon known as overbidding. When participating in an auction, brain areas sensitive to loss become active. When the authors modified the ground rules of the auction so as to emphasize the potential for loss, without altering the basic possibility of winning, the tendency to overbid was magnified.

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John Edward Porter is a former U.S. congressman who chaired the Appropriations subcommittee that funds all federal health programs, including NIH. He is chair of ResearchAmerica and chaired the U.S. National Academy of Sciences committee that has just published a report advising presidential candidates on science and technology appointments.*

If All You Do Is Vote ...

ELECTIONS HAVE A WAY OF SORTING THINGS OUT. ALREADY, THE MOST FASCINATING U.S. presidential and congressional election process of my life has sorted out some things that we can celebrate. We know that the country's next president won't favor teaching intelligent design in our schools and will respect scientific integrity and evidence-based research. But we still don't know whether he will truly put science at the table—that is, whether research will be high on the president's priority list and reflected strongly in his budgets, speeches, and policies.

So what can U.S. scientists do to substantially increase the probability that we will have elected officials who will make research a very high priority? I'm talking about much more than voting on Election Day, paying dues to a professional society, or making a contribution to a voluntary health association. And here's why.

For the past 7 years, the United States has had a presidential administration where science has had little place at the table. We have had a president opposed to embryonic stem cell research and in favor of teaching intelligent design. We have had an administration that at times has suppressed, rewritten, ignored, or abused scientific research. At a time when scientific opportunity has never been greater, we have had five straight years of inadequate increases for U.S. research agencies, which for some like the National Institutes of Health (NIH) means decreases after inflation.

All of this has been devastating for the scientific community; has undermined the future of our economy, which depends on innovation; and has slowed progress toward better health and greater longevity for people around the world. So if you are a U.S. scientist, what should you do now?

First, help identify candidates for the next president's science appointments. They range across a variety of agencies and departments, and the U.S. National Academies have listed those viewed as most important.* Urge your distinguished colleagues to serve our nation in this way, and help the scientific community to support them.

Second, in choosing candidates who are running for Congress or even state office (often, state officials will later run for federal office), volunteer to advise those candidates on science matters and issues. They'll love it! Offer to serve on their science advisory committee. If they don't have one, tell them you'll create one. Chair it yourself and recruit suitable colleagues. Once your candidate has won the election, offer to continue in your role as a science adviser. Wouldn't it be wonderful if all candidates had science advisers or science advisory committees? They will, if individual scientists step up to the plate.

Third, school yourself on the candidates and their positions on science issues. Visit science voter education resources, like YourCandidatesYourHealth.org, which asks all federal candidates to answer questions about their positions on science and health. If your candidates have not responded, call their campaigns and ask them to do so. You have a right to know where they stand.

Fourth, encourage debates about science among those who seek public office. Go to their debates and raise science questions. Sign onto ScienceDebate2008.com, which urges the presidential candidates to have a debate dedicated to science issues. Even though this won't happen now, support for this initiative will send a message to the media and the candidates that science is important to the electorate and that the questioners should include science in the debates.

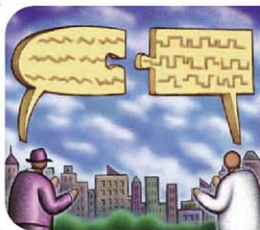
And last but not least, next time run for office yourself! It's disheartening to see so many public officials with little knowledge of science. Bill Foster, a physicist, recently won the House seat of former Speaker Dennis Hastert. You can do it, too.

Your country needs you. If all you do is vote, you're definitely not doing enough. Get off your chair, do something outside your comfort zone, and make a difference for science. All of us must be creative about what we can do to make a difference for the things we believe in. Now is the time.

—John Edward Porter

10.1126/science.1163096

*Science and Technology for America's Progress: Ensuring the Best Presidential Appointments in the New Administration, www.nap.edu/catalog.php?record_id=12481.



CELL BIOLOGY

A New Way in

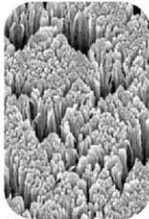
Many cellular stimuli induce signaling cascades that terminate with a protein entering the nucleus to activate transcription of target genes. Most of these proteins contain a conserved stretch of amino acids known as a nuclear localization signal (NLS), which binds to the nuclear import factor importin alpha, and the complex translocates into the nucleus through the nuclear pores. However, the absence of an NLS in some signaling proteins suggested that they access the nucleus via alternative mechanisms. Now, Chuderland *et al.* find a new signal in the extracellular signal-related kinase 2 (ERK-2). A three-amino acid domain is phosphorylated upon stimulation, allowing the protein to bind to a different nuclear import factor, importin 7, and enter the nucleus. A similar domain was found in other cytonuclear shuttling proteins, and the same phosphorylation-dependent mechanism was shown to occur for nuclear accumulation of SMAD3 and MEK1. Thus, this domain acts as a general nuclear translocation signal and represents a new mechanism whereby proteins can enter the nucleus. — HP*

Mol. Cell 31, 10.1016/j.molcel.2008.08.007 (2008).

CHEMISTRY

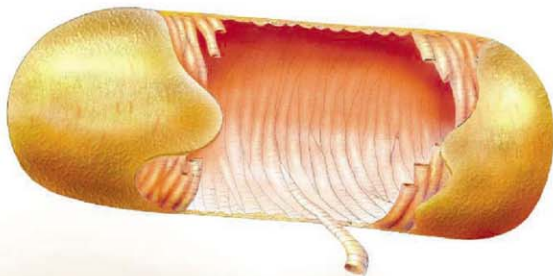
More Surface, More Reactivity

To gain a better understanding of palladium's reactivity as a hydrogenation catalyst, many model studies that use well-defined single-crystal surfaces have focused on what should be the simplest substrate, ethylene. Although this reaction is



facile for reactant pressures near ambient, at very low pressures (ultrahigh-vacuum conditions), the reactivity on close-packed surfaces is low (yields of ethane <1%), and not much greater on supported nanoparticles (<5%). This difference is attributed to a lack of surface hydrogen caused by absorption into

*Helen Pickersgill is a forum editor in Science's editorial department.



CELL BIOLOGY

Growing Through a Wall

In bacteria, the cell wall must be firm enough to define cell shape and allow a high internal osmotic pressure, while at the same time sufficiently dynamic to allow cell growth and division. Hayhurst *et al.* provide insight into how the cell wall in the rod-shaped organism, *Bacillus subtilis*, is structurally organized to achieve these functions. The main structural component of the cell wall is peptidoglycan, comprising glycan strands cross-linked by peptides. Atomic force microscopy (AFM) on purified glycan revealed individual strands up to 5 μm long (5000 disaccharides). Fluorescence microscopy in whole cells showed that *B. subtilis* displays very few terminal *N*-acetyl glucosamine (GlcNAc) residues and that internal peptidoglycan-associated GlcNAc residues exhibit a pattern suggestive of a helical structure. AFM imaging of *B. subtilis* peptidoglycan sacculi revealed little indication of structural features on the outer surface, probably because surface layers are hydrolyzed during cell wall turnover. However, the inner surface exhibited 50-nm-wide cables running across the short axis of the cell with cross striations consistent with a helical structure. The authors suggest that during biosynthesis, glycan strands are polymerized and cross-linked and then coiled to form the inner-surface cables. New helices are likely inserted into the cell wall by being cross-linked between two existing cables, while the external surface is cleaved to allow cell growth. — VV

Proc. Natl. Acad. Sci. U.S.A. 105, 14600 (2008).

DEVELOPMENT

Protected by a Maelstrom

Germ-line cells could be considered the most precious in the body, because they are the only cells to contribute directly to the next generation. Hence, special mechanisms should be in place to protect them from damaging agents such as transposable elements. Cells in many species silence these elements by using small noncoding RNAs. The RNA interference factors localize to perinuclear structures called nuage in germ cells. Soper *et al.* focus on a murine homolog of *Drosophila* maelstrom (*mael*), a gene that functions in the production of interfering RNAs, repression of transposable elements, and speci-

the bulk. Dohnálek *et al.* have prepared model catalysts through ballistid deposition of Pd atoms at cryogenic conditions (22 K) and glancing angles such that one-quarter of the atoms are surface exposed. The as-prepared nanoporous films showed much higher reactivities (50%), which decreased when the films were densified by reaction cycles that went to room temperature (with ethane desorbing by 250 K) or after annealing to higher temperatures. The authors note that although surface roughening treatments can also create a large number of active sites, the low fraction of bulk atoms in the nanoporous films limits removal of hydrogen from the surface and boosts overall reaction rates. — PDS

J. Phys. Chem. C 112, 10.1021/jp803880x (2008).

cation of the *Drosophila* oocyte axis. Similarly, the murine *Mael* gene is localized stage-specifically to the nuage structures in male germ cells. Eliminating *Mael* from mice resulted in defective meiosis due to abnormal chromosome synapsis and massive DNA damage. A mechanism for meiotic failure is demonstrated through *Mael*'s function in transcriptional repression of transposable elements via a DNA methylation mechanism. — BAP
Dev. Cell 15, 285 (2008).

CELL BIOLOGY

NE-ER Shape Shifting

Mitosis in metazoans involves the wholesale disruption of normal cellular architecture to allow for successful partitioning of cellular components to each daughter cell. During most of the cell cycle, the nucleus is surrounded by a double-membraned nuclear envelope (NE) that is contiguous with the endoplasmic reticulum (ER), an intracellular labyrinth of interconnected tubules and sheets. Anderson and Hetzer have examined the processes involved in the dramatic rearrangements of the NE and ER at the end of mitosis. The NE is disassembled at the beginning of mitosis and, after the partitioning of chromosomes, must be reassembled to form two daughter cells complete with their own NE-enclosed nuclei. By quantifying images produced using time lapse microscopy, the authors were able to observe the recruitment of ER tubules to chromatin, which went on, within ~12 min, to produce membrane-enclosed daughter nuclei capable of performing nuclear import.

Increasing the expression of ER tubule-promoting proteins interfered with the formation of new nuclei, whereas reducing their expression sped up the process, which may suggest that it is the transition of ER from tubules to sheets that limits NE assembly and nuclear expansion. Thus, ER architectural proteins play a key role in nuclear reconstruction and NE assembly after mitosis. — SMH

J. Cell Biol. 182, 911 (2008).

CLIMATE SCIENCE

A Hurricane History

One problem in assessing whether recent climate change has significantly influenced either the strength or frequency of hurricanes and tropical storms is that in general, these factors

have been measured systematically only recently. Thus, establishing a reliable baseline to compare with present trends has been difficult. In the Lesser Antilles—one of the first areas settled heavily in the New World, and a focus of early trade—British ships' logs, newspaper accounts, official colonial correspondence, and other sources provide a variety of data over the past 300 years or so. Chenoweth and Divine used these sources to derive a historical record of hurricanes, tropical storms, and tropical depressions in this region, which is along the main track of storms that eventually develop and hit the United States and Mexico. The authors identified 550 tropical storms and hurricanes passing through these islands, about half of which were not previously detected, including in more recent records. Overall, there seems to be no discernible trend in activity since 1690, though the period from 1968 to 1977 had notably few storms. — BH

Geochim. Geophys. Geosyst. 9, 10.1029/2008GC002066 (2008).

BIOCHEMISTRY

SH2 Uninhibited

Src-homology 2 (SH2) domains of cytoplasmic tyrosine kinases have an important and well-defined role in keeping such kinases in an autoinhibited conformation. Filippakopoulos *et al.* studied the human cytoplasmic tyrosine kinase Fes, which lacks this autoinhibitory interaction, and uncovered molecular details of how SH2 domains can alternatively act to enhance activity. The authors solved crystal structures of a portion of Fes containing the SH2 domain and kinase domain, with and without phosphorylation of the kinase activation segment. This fragment was bound in complexes with a substrate

peptide and an ATP-mimetic kinase inhibitor. Mutagenesis experiments confirmed that the visualized interaction of the SH2 domain with the kinase domain was necessary to stabilize the active conformation of the enzyme. Analysis of synthetic substrates with or without phosphorylated SH2 domain-binding sites also showed the importance of the SH2 domain in substrate recruitment. Extending the analysis to the pro-oncogenic tyrosine kinase c-Abl showed that a similar mechanism occurs in other members of the cytoplasmic tyrosine kinase family. The authors point out that such coupling of substrate recognition to kinase activation may contribute to selectivity of such kinases so that they act only on the appropriate substrates *in vivo*. — LBR

Cell 134, 793 (2008).



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The Galápagos' Lost and Found

Of the 15 species of the iconic Galápagos giant tortoise, four have already gone the way of the dodo. Charles Darwin wrote about the relentless culling of one now-extinct species on Floreana Island, *Geochelone elephantopus*, for food and lighting oil. In a second chapter of this story, a team from Yale University reported in this week's *Proceedings of the National Academy of Sciences* that they have found 13 descendants of this species alive and well on neighboring Isabela Island.

"It's strange that the human activities responsible for depleting this population have allowed it to survive elsewhere," says senior author Gisella Caccone. She theorizes that whalers left the tortoises on Isabela's highest summit, Volcan Wolf, as a larder to feed them on a return trip.

By comparing the DNA from 93 Volcan Wolf tortoises with that of museum specimens, the team discovered that 13 had some Floreana lineage. "It's extraordinary to find descendants of a species when it already has gone extinct," says George Amato, director of conservation genetics at the American Museum of Natural History in New York City. Caccone says it may even be possible to resurrect the species in captivity by selectively breeding out the Isabela genes.



Northeasterners scored highest on the neuroticism and openness scales but were not particularly conscientious or agreeable. Denizens of the Midwest and the South had the highest conscientiousness and agreeableness ratings. For extraversion, the Midwest, the South, and the Great Plains states ranked highest,

Rentfrow reported in a paper published online this month in *Perspectives on Psychological Science*. Although participants were slightly younger than the general population, their racial and gender breakdown mirrored that of the country, Rentfrow says.

The study is the latest in a growing field that uses the Internet to study aggregate personality traits of entire populations. Robert McCrae, a psychologist at the National Institute on Aging in Bethesda, Maryland, who studies personality differences between countries, calls the study "a very ambitious attempt to get at a new way of analyzing personality data."

WoW! NSF Funded What?

Bloggers have been heaping scorn on the U.S. National Science Foundation (NSF) for awarding \$100,000 to computer scientist Bonnie Nardi of the University of California, Irvine, to study the popular role-playing computer game *World of Warcraft* (WoW).

Users can freely make add-ons to the basic WoW software, and Nardi wants to know why American users edit the software more often than their Chinese counterparts do. But WoW players say they already know the answer: As one wrote in a post to the Web site GamePolitics, "More Americans play WoW on computers they own. More Chinese players play at internet cafes and computer centers."

But NSF is sticking up for its grant. "While we have previously supported research on highly formalized open-source software development," says NSF program officer William Bainbridge, "this may be the first study we have supported on how software is developed in the nearly complete absence of formal organization."

True to Stereotype

Behind every stereotype lies a kernel of truth, the saying goes. A recent study of regional personality differences in the United States seems to agree. Jason Rentfrow, a psychologist at University of Cambridge, U.K., invited Internet users across the United States to take a survey devised to assess psychology's "Big Five" personality dimensions: openness, conscientiousness, extraversion, agreeableness, and neurotic tendencies, such as anxiety.

More than 619,000 people responded. Breaking the responses down by state, Rentfrow found that personality traits clustered by region:

"Neurotic"
NYC cabbie?



Books have been written about "near-death" experiences—visions of tunnels and figures of light or accounts of hovering over the operating table watching doctors bang on their chests—occurring when a patient's heart and brain have stopped functioning. Now, a British physician is spearheading a large-scale project aimed at finding out what's going on.

The study of Awareness During Resuscitation, sponsored by the University of Southampton, U.K., was announced this month at a United Nations symposium on consciousness by project leader Sam Parnia, a resident at New York–Presbyterian Medical Center. Parnia has recruited 25 hospitals, mostly in the United States and the United Kingdom, to monitor as many as 1500 people during cardiac arrest who then survive to tell about it. "About 10% of such people report some kind of cognitive process" while "dead" for a few seconds to more than an hour, Parnia says.

Psychiatrist C. Bruce Greyson of the University of Virginia, Charlottesville, says emergency rooms and intensive-care units will measure oxygen flow to patients' brains and will test their blood for proteins released when brain cells die. Researchers will also ascertain whether patients accurately describe things from their out-of-body experiences that they could not have seen.

What if the phenomenon proves real? "I think that shows that the current understanding of brain and mind"—that to have such experiences you need "a coherent neural network involving a good portion of the cortex"—is "inadequate," Greyson says.



DIGGING FOR CLUES. Virologist John Oxford of Barts and The London School of Medicine and Dentistry in the United Kingdom hopes that exhuming the body of a British politician felled by the Spanish flu after World War I will yield important clues to dangerous modern-day strains.

Although tens of millions died in the 1918-19 epidemic, Oxford (inset) homed in on Mark Sykes, who helped draw up national boundaries after the collapse of the Ottoman Empire, because he assumed his lead-lined

coffin—pricey and rare for its time—would have kept the body from decomposing completely. Although the Sykes family readily gave its consent, Oxford spent 3 years on the paperwork to get the excavation approved. When he finally unearthed Sykes at the East Yorkshire gravesite last week, the body was, as Oxford had hoped, well enough preserved to obtain useful tissue samples. It will take another 4 months of biosafety-level 4 lab procedures before any data emerge.

A SPECIAL LASKER. A half-century spent as a microbe hunter has earned Stanley Falkow the 2008 Lasker-Koshland Award for Special

Achievement in Medical Science. The award, renamed this year to honor Daniel E. Koshland Jr., recognizes Falkow's discovery of the molecular nature of antibiotic resistance, his work on new methods to

by which bacteria survive and spread, and his mentoring of more than 100 students.



BEETLE SOUP. A field trip to collect beetles from the Himalayan foothills has turned into a legal nightmare for Czech entomologist Petr Švácha and his assistant Emil Kučera.

The two men spent a month in an Indian jail and were found guilty of collecting biological specimens without a permit. On 10 September, a judge let Svācha off with a \$500 fine. But his ordeal is not over yet. Indian forestry officials have said that they may appeal to a higher court to send him to prison. Kúčera, whose personal Web site included an offer to provide insect specimens to interested parties, was sentenced at the same time to 3 years in prison and fined \$1500. He is appealing the verdict.

Hoping to collect specimens while avoiding the notorious Indian bureaucracy, the duo went to India as tourists in June and assumed they would be fine as long as they avoided protected

areas such as national parks. But they ran afoul of a 2002 law that requires permits for collecting natural specimens anywhere in the country and were arrested 22 June. Indian researchers have also complained about that law. "Biologists should start defending themselves against the attacks of bureaucrats and attempts to enclose biology in political borders," Svácha says.

WORKPLACE ACCIDENT. A German physicist in charge of a gamma-ray telescope that was to have been inaugurated last week fell to his death from 8 meters while calibrating the instrument. Florian Goebel, 35, had been the project manager for MAGIC II—built on a La Palma mountaintop in the Canary Islands—since 2005.

Officials from the 17 institutes across Europe and the United States that are part of the MAGIC (Major Atmospheric Gamma-ray Imaging Cherenkov Telescope) collaboration are investigating the circumstances of his



death on the night of 10 September.

"Goebel was an expert and knew all [safety] rules and procedures," says Masahiro Teshima, spokesperson for the collaboration. "We don't understand how this could happen."

Goebel had worked at the German DESY research center for particle physics before joining the Max Planck Institute for Physics in Munich, the main German partner. "He was a very talented and cheerful person and an extremely good scientist," says Teshima. "Everybody loved him."

Together with an almost identical telescope completed 5 years ago, MAGIC II will study atmospheric particle showers created by high-energy cosmic gamma rays. Its inauguration has been postponed until next year.

David Korn, a former Stanford University medical school dean who has been a prominent voice in Washington, D.C., for the biomedical research community, will become Harvard University's first vice provost for research. Korn has served since 1997 as senior vice president for biomedical and health sciences research at the Association of American Medical Colleges, weighing in on everything from research funding to financial conflicts of interest. Starting in November, he will develop research policies for Harvard's schools and affiliated hospitals as part of efforts to promote collaboration. At 75, Korn could have hung up his boots, but he says he was looking forward to another challenge. "Everything I've done in my career has been engrossing and stimulating. This position could be a splendid, probably last, stage," he says.



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More overruns for Mars lander

1754



Q&A with Britain's science adviser

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SCIENCE EDUCATION

Misjudged Talk Opens Creationist Rift at Royal Society

A talk titled "Should Creationism Be a Part of the Science Curriculum?" was bound to attract attention at the annual meeting of the British Association for the Advancement of Science (BA) earlier this month. But last week, it cost the speaker, Michael Reiss, his job as director of education at the Royal Society, Britain's academy of science.

Within hours of his 11 September talk, news items appeared on the Internet claiming that Reiss had urged science educators to teach creationism, although many attending the speech said that he had clearly not made such a call. His comments—or perhaps more accurately the spin placed on them by headline writers, newspaper columnists, and editorialists—ignited a firestorm. Several prominent scientists, including a trio of Nobel laureates, called for his resignation. The Royal Society hastily put out a statement defending Reiss but 4 days later issued another statement announcing his resignation and leaving the clear impression he had been forced out.

Although some critical of Reiss applauded his sudden exit, others saved their harsh words for the organization he left. "This has damaged the Royal Society, the way they handled it," says Derek Bell, head of the Association for Science Education in the United Kingdom.

On paper, Reiss, who remains a professor at the University of London's Institute of Education, seemed the perfect speaker at the science festival in Liverpool. In addition to having a doctorate in science education, he's an ordained minister in the Church of England and coedited the book *Teaching About Scientific Origins: Taking Account of Creationism*. In his 11 September talk, Reiss noted that teachers are bound to encounter pupils with creationist views. If these are brought up in class, he argued, simply dismissing them as not appropriate to a science lesson will only alienate those pupils. Instead, Reiss advocates taking the opportunity to explain the difference between the creationist viewpoint, which, he emphasizes, has no evidence to

support it, and evolution, which, he says, has a lot. A teacher's answers to such questioning from creationist pupils "can be used to illustrate a number of aspects of how science works," Reiss says in the online text of his talk (www1.the-ba.net/bafos/press/showtalk2.asp?TalkID=301).

Efforts by creationists or believers in intelligent design to tamper with school science



Wise words? Reiss's comments on dealing with creationist pupils were jumped on by U.K. newspapers.

curricula are viewed in Europe as largely an American phenomenon, one reflected in the public acceptance of the theory of evolution. Only about 40% of adults in the United States accept the idea of Darwinism, compared with about 70% in the United Kingdom and many other European nations (*Science*, 11 August 2006, p. 765). Yet throughout Europe, groups promoting creationist views are emerging from Protestant, Catholic, and Islamic communities in different countries.

In the United Kingdom, government pol-

icy throughout this decade has been to create more so-called faith schools, high schools funded predominantly by government but managed by religious organizations. This has increased concern among science educators about the spread of creationism into curricula. There was also widespread condemnation in 2006 of a pressure group called Truth in Science that sent creationist teaching materials to every U.K. high school. In part because of this, in 2007 the government published guidance for schools on how to address creationism and intelligent design, drafted by Reiss and others.

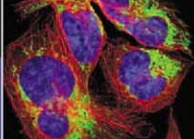
The day after his speech, Reiss was greeted by headlines such as "Call for creationism in the classroom," in the *Financial Times*, and "Children should be taught about creationism in school," in the *Daily Mail*. Highlighting Reiss's description of creationism as a "worldview" that should be respected, many of the stories suggested he equated it with the theory of evolution. That same day, the Royal Society issued a statement reaffirming its position that creationism should not be taught as science, saying that Reiss's views had been "misrepresented" and offering a clarification from him.

That move failed to quell the storm. Several fellows of the Royal Society stated publicly that it wasn't appropriate for Reiss to hold such an influential position given his religious affiliation. "I do not see how he could continue," says Nobelist Harry Kroto of Florida State University in Tallahassee. On 13 September, another society fellow, Nobelist Richard Roberts of New England Biolabs in Ipswich, Massachusetts, sent a letter to the Royal Society, cosigned by Kroto and John Sulston of the University of Manchester in the U.K., calling

for Reiss to step down.

Reiss has declined to comment since his talk, but on 16 September the society issued a new statement, saying that Reiss's comments "were open to misinterpretation. While it was not his intention, this has led to damage to the Society's reputation." The society and Reiss, the statement continued, had agreed that "in the best interests of the Society, he will step down immediately."

Scientists and experts in science education have leapt to Reiss's defense. "There's an awful



lot of support for Michael Reiss, as a person and his views," says Bell. Fertility expert and society fellow Robert Winston of Imperial College London issued a statement critical of the Royal Society: "This is not a good day for the reputation of science or scientists. This individual was arguing that we should engage with and address public misconceptions about science—something that the Royal Society should applaud." Even evolutionary biologist and noted creationism critic Richard Dawkins defended Reiss on his Web site, call-

ing efforts to remove him "a little too close to a witch-hunt."

Others, however, welcomed Reiss's departure as the best way for the Royal Society to make clear its position on creationism. "The only reason to mention creationism in schools is to enable teachers to demonstrate why the idea is scientific nonsense," says Christopher Higgins, vice-chancellor of Durham University in the U.K.

Royal Society President Martin Rees said in an e-mail to *Science* that "the Royal Soci-

ety should be secular, but not anti-religious." But Phil Willis, a member of the U.K. Parliament who chairs a committee that oversees British science, acknowledges that there is a "very stark division" between those in the society who reject religion completely and those who urge coexistence or are themselves religious. Although Willis has great respect for Reiss, he was "caught making injudicious comments," Willis says. "It's a real tragedy, [but] it's inevitable that they parted company."

—DANIEL CLERY

PARTICLE PHYSICS

After Spectacular Start, the LHC Injures Itself

When physicists first sent particles racing through the world's biggest atom smasher on 10 September, the Large Hadron Collider (LHC) at the European particle physics laboratory, CERN, near Geneva, Switzerland, the gargantuan machine purred like a kitten. But only 9 days later, the LHC proved it can also be a temperamental tiger, damaging itself so severely that it will be out of action until next spring.

It all seemed so easy earlier this month when after just a few hours researchers had beams of protons whizzing through both of the 27-kilometer-long, \$5.5 billion machine's countercirculating rings. That smooth start raised hopes that the LHC would start colliding particles as early as this week. But last Friday, some of the 1232 main superconducting dipole magnets, which keep the beams on their circular trajectories, abruptly overheated in an event known as a "quench." The incident ruptured the plumbing that carries liquid helium through the magnets to chill them to 2 kelvin—2 degrees above absolute zero.

The quench highlights the LHC's ability to injure itself, says Reinhard Bacher of the DESY particle physics lab in Hamburg, Germany. Compared with earlier colliders, "the LHC is operating in all aspects much more at the critical edge," he says. The breakdown raises the question of whether a key protection system worked properly.

A superconducting magnet is

essentially a coil of superconducting wire that generates a magnetic field when current flows through it. If kept extremely cold, the wire carries huge currents without resistance; a quench occurs when part of it overheats and acts like an ordinary wire. The hot bit serves as an electric heater that can trigger a runaway reaction, toasting the rest of the magnet and converting the energy in its field to heat.

Such an event can start if, for example, protons stray out the beam pipe and into the magnet material. The 19 September quench occurred a different way, however. Within the LHC, the 15-meter-long magnets are connected so that current from one magnet flows into the next. With no beam, researchers were ramping up the current in a chain of 154 dipole magnets when the superconducting connection between two magnets apparently overheated and melted, says CERN spokesperson James Gillies. That breach can also cause an uncontrolled quench. The loss of current causes a magnet's field to quickly ebb. However, the magnet will produce a voltage surge

to counteract the waning of the field. The reaction can then heat the magnet as a whole.

The field of an LHC dipole contains a whopping 8.6 megajoules of energy, enough to melt 42 kilograms of copper or to cook the magnet in a fraction of a second. Researchers designed a quench-protection system to quickly shunt current out of an afflicted magnet and into large steel blocks. Ironically, it also heats the entire magnet to spread out the toll from the quench. During last Friday's mishap, the quench-protection circuits fired as expected, Gillies says.

Nevertheless, the broken helium line suggests that at least one \$900,000 magnet was ruined and will need to be replaced. "I cannot tell if any of the safety systems failed," says CERN's Rüdiger Schmidt, who leads the machine-protection team. "It is absolutely too early to tell."

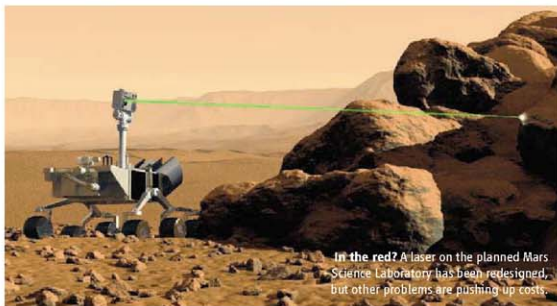
To make repairs, researchers will have to warm up an entire octant of the LHC and then cool it back down. Bacher says that DESY researchers experienced similar delays when they commissioned their HERA collider, which smashed electrons into protons from 1992 to 2007. "We had three or four of these warm-up-and-cool-down cycles," he says. One such cycle will take at least 2 months for the LHC. That will run into a planned shutdown for the winter, when the cost of power climbs, so experimenters will have to wait until next spring to collect data.

—ADRIAN CHO



Hot spot: A worker looks up LHC magnets. The machine broke down when an electrical link between two magnets melted.

CREDIT: CERN



In the red? A laser on the planned Mars Science Laboratory has been redesigned, but other problems are pushing up costs.

SPACE SCIENCE

Rising Costs Could Delay NASA's Next Mission to Mars and Future Launches

Faced with a dramatically higher price tag, NASA managers will decide next month whether to postpone the launch of a sophisticated Mars rover for 2 years. Such a delay in the Mars Science Laboratory (MSL) would mark a significant setback to the Mars research program, which has sent a new spacecraft to the planet every other year for a decade. Planetary scientists also worry that pushing back the mission could have a ripple effect, delaying and even canceling future missions.

The science laboratory, currently slated for launch in the fall of 2009, is four times heavier than the current rovers trundling across the planet's surface. It features a plethora of advanced tools and instruments designed to analyze rocks, soil, and atmosphere. But that complexity has led to technical troubles and higher costs. When proposed in 2004, the lab was expected to cost \$1.2 billion. By this summer, that price tag had climbed to \$1.9 billion, and last week NASA space science chief Edward Weiler warned that "there is another overrun coming." Another NASA official put the latest increase at approximately \$300 million.

Engineers at NASA's Jet Propulsion Laboratory (JPL) in Pasadena, California, which is responsible for MSL, are now working overtime to prepare the spacecraft for environmental testing and launch. Weiler and NASA Administrator Michael Griffin will pore over those results and the latest cost estimates when they meet in mid-October to determine whether to delay the mission. In addition to

worrying about the unbudgeted overtime, Weiler is concerned that engineers may be rushing their inspection of the rover's complicated systems. "The alternative could be that we get a crater on Mars," the science chief adds ominously, evoking previously failed missions to the Red Planet.

"Postponing MSL is a real possibility, and an unfortunate one," says Brown University planetary scientist Jack Mustard, who also chairs NASA's Mars science advisory panel. "A 2-year delay could increase the cost of the mission significantly—and that would come out of the Mars budget." He also fears that this could slow momentum for Mars exploration and jeopardize plans for a 2016 rover and a sample-return mission.

MSL's cost and technical woes began in earnest last year, when NASA considered jettisoning two instruments, ChemCam and the Mars Descent Imager. ChemCam, an instrument designed by French and American researchers that would use a laser to vaporize martian rock and dust for spectrographic analysis and take detailed photographs, proved more expensive than anticipated. In a compromise reached last fall, NASA provided extra money to complete a simplified version of the instrument. The Mars Descent Imager, a camera designed to provide a view from just above the surface of the rover's landing site, was canceled but revived when engineers found ways to control costs by making relatively

minor changes.

But those changes didn't stanch the financial bleeding. The latest technical problems affecting the MSL budget include the tardy delivery of hardware used in the sample acquisition and handling portion of the laboratory. NASA Planetary Science Division Director Jim Green said in June that the total overrun for MSL in 2008 and 2009 was \$190 million. Most of that money—some \$115 million—will come from other MSL-related projects. JPL spokesperson Guy Webster referred MSL questions to NASA headquarters.

A new \$300 million overrun, says a NASA official familiar with MSL, could force the agency to cancel the \$485 million 2013 Scout mission announced just last week to probe the planet's atmosphere (*Science*, 19 September, p. 1621) or the 2016 Mars mission. "Rest assured the Mars program has to pay for this," the official added.

Mustard, who last week chaired a Mars advisory panel session in California, says there is growing anxiety in the community about the implications of an MSL delay on an exploration program that began in the late 1990s. "If you delay it until 2011, then you might lose the 2016 mission," he says. The 2016 Mars effort now under consideration likely would be a smaller rover that could include some sample-gathering technology designed to test systems for an eventual sample-return mission from Mars to Earth. The projected \$1.4 billion cost of such a rover would fall between MSL and the current Spirit and Opportunity rovers now on the surface.

NASA's former space science chief, S. Alan

Stern, who resigned in protest this spring after a disagreement with Griffin over how to deal with cost overruns (*Science*, 4 April, p. 31), last year proposed a Mars sample-return mission to arrive at the end of the next decade. But static

budgets, spacecraft overruns, and the need to conduct other missions make that increasingly unrealistic, say agency managers and academic researchers. Weiler notes that a sample-return mission would cost many billions of dollars and that NASA is planning first to launch a mission to either Jupiter or Saturn late in the next decade. And although scientists are intrigued by the idea of a sample-return mission, they see it slipping into the more distant future.

"Plans for a sample return were smoke and mirrors," says Mustard. "It's a good idea—but where's the money?"

—ANDREW LAWLER

With reporting by Richard A. Kerr.

GEOCHEMISTRY

Geologists Find Vestige of Early Earth—Maybe World's Oldest Rock

Really old stuff is rare on Earth. The planet's brand of violent geology has just been too dynamic to preserve much from its earliest days. Formed 4.567 billion years ago, Earth has yielded 4.3-billion-year-old mineral grains and 4.0-billion-year-old rocks that hint at how a ball of primordial debris evolved into a crustal-over, largely ocean-covered abode of life.

So geologists keep searching the oldest, most brutally battered terrains for more traces of earliest Earth. On page 1828, a group reports the discovery of rock in northern Quebec on Hudson Bay that records the existence of the earliest crust. The Canadian rock may also be the oldest known rock by 300 million years.

Given how beaten up the oldest rocks are, geologists often fall back on atomic-scale records preserved in the isotopic and elemental composition of the rocks. Geologist Jonathan O'Neil of McGill University in Montreal, geochemist Richard Carlson of the Carnegie Institution of Washington's Department of Terrestrial Magnetism in Washington, D.C., and colleagues analyzed isotopes of the elements samarium and neodymium from the Nuvvuagittuq greenstone belt of northern Quebec. These isotopes can be used to trace geologic processes because some isotopes are stable and don't change no matter how many eons pass, whereas some steadily decay radioactively into other, more stable isotopes. Different elements behave differently when rock partially melts; some tend to concentrate in the melt, while others remain behind.

Delving into the samarium and neodymium of volcanic and altered sedimentary Nuvvuagittuq rock, O'Neil and his colleagues found isotopic signs that the rock could represent the oldest section of crust on Earth. Geochemists had already found rock in Greenland that, according to its isotopes, had been derived from the earliest mantle rock. But by 4.3 billion years ago, that mantle rock had partially melted to yield crustal rock, so researchers had

figured "protomantle" by analyzing Greenland rock derived from it. But where was the "protocrust" that must have been formed as the protomantle formed?

O'Neil and colleagues think they now have such protocrust in Quebec. The Nuvvuagittuq rock has the opposite neodymium isotope signature of the Greenland rock's protomantle. Either this rock is a 2-kilometer-long sliver of protocrust resembling today's iron-rich ocean crust, or it was derived from such protocrust. "That's a first," says geochemist Albrecht Hofmann of the



Older than dirt. Rocks by Hudson Bay may date back to when Earth first separated its primordial stuff into mantle and crust.

Max Planck Institute for Chemistry in Mainz, Germany. "It's an heroic effort" to measure the subtle isotopic variations involved.

The group goes further, drawing on the clocklike radioactive decay of samarium-146 to calculate an age of formation of the Nuvvuagittuq rock of about 4.3 billion years. If accurate, that age would mean they have the protocrust itself, not just something derived from it. That rock would be the oldest rock known, approaching the age of individual zircon mineral grains from western Australia that tell of a wet and weathered world soon after Earth's origin. The new age "is exciting," says geochemist Mukul Sharma of Dartmouth College, but uncertainties remain about details of the rocks' formation that bear on its isotopic age. "There's a lot more work that needs to be done," he says, before a new world's most ancient rock can be crowned.

—RICHARD A. KERR

EPA Nixes Perchlorate Standard

After a multiyear bureaucratic fight, the U.S. Environmental Protection Agency (EPA) has decided not to regulate a toxic rocket fuel component leaching into the nation's drinking water. The proposed ruling explains that requiring the cleanup of perchlorate, which is polluting areas near U.S. military sites, would provide no "meaningful opportunity for health risk reduction." It's a controversial decision. "There is substantial evidence that this chemical needs to be regulated," says toxicologist Melanie Marty, chair of EPA's child health advisory committee. In a 2006 letter to EPA, Marty cited studies that suggest current perchlorate levels at hundreds of U.S. sites could "result in exposures that pose neurodevelopmental risks" to infants.

—ELI KINTISCH

Scientists Go Nano a Mano

Last week, the U.S. Environmental Protection Agency and the National Science Foundation jointly funded two centers to track the environmental implications of nanomaterials for 5 years. A \$24 million center led by the University of California, Los Angeles, will perform cell-based studies to find materials that pose the greatest potential risks. The other center, awarded \$14 million and led by researchers at Duke University in Durham, North Carolina, will track the effects of nanomaterials on organisms as they move through tightly controlled ecosystems in labs. Andrew Maynard, a nanotechnology expert with the Woodrow Wilson International Center for Scholars in Washington, D.C., says the work "is an important step." But he would prefer to see a "robust federal risk research strategy" to systematically evaluate dangers from all potential nanomaterials. —ROBERT F. SERVICE

Gray Wolf Regains Protection

The U.S. Fish and Wildlife Service has put the gray wolf back on the endangered species list. The listing conforms to a U.S. district court order issued in July (*Science*, 25 July, p. 475). There had been speculation that the government might appeal the ruling, which came after the Natural Resources Defense Council and other groups challenged a February decision by the agency to delist the Northern Rockies wolves. Now scientists with the council say they're cautiously optimistic about the wolf's chances. Two thousand wolves roam the region, they calculate; more than 2500 are needed for proper genetic mixing.

—ELI KINTISCH

JOHN BEDDINGTON INTERVIEW

U.K. Science Adviser Makes His U.S. Debut

WASHINGTON, D.C.—Last week, during his first visit to the United States as the U.K. government's chief scientific adviser, John Beddington sat down with *Science's* news editors to discuss topics as varied as food, fuel, and physics. Nine months into his job, Beddington has adopted a lower profile than his headline-grabbing predecessor, David King. A population biologist at Imperial College London, Beddington has specialized in applying biological and economic tools to questions of natural resource management, particularly fisheries (*Science*, 22 June 2007, p. 1713). He's no stranger to politics, having advised the British government, the European Commission, the United Nations Environment Programme, and its Food and Agriculture Organization. Now Beddington must answer questions from the prime minister and Cabinet, as well as coordinating the science advice in all government departments and chairing a number of committees. The following excerpts from his interview were edited for brevity and clarity.

—DANIEL CLERY

Q: If you could put one file in the new U.S. president's in-tray, what would it be?

Online

[sciencemag.org](http://www.sciencemag.org)

Read an extended interview on *ScienceNOW*.

J.B.: The message I would probably want to give is the intimate connection between the issues of climate change, food security, energy security, and water security. These issues need mixed approaches; they need a mix of both science and engineering. These issues are tremendously important because they are going to come quite quickly. The sort of demand increases that are to be expected from urbanization, movement out of poverty, and population growth are quite dramatic, on a time scale of only a couple of decades.

Q: One of David King's goals was to increase the use of science advice across all government departments. Is that job done?

J.B.: I've done a number of things that are slightly different from David. Every 6 weeks, all of the Chief Scientific Advisors of the major departments dealing with science meet with me and with each other. We form subgroups: One is dealing with climate change and food security issues and another is going to be dealing with infectious diseases. That's a good bit of networking. In addition, this group is now meeting with the chief executives of the research councils every 3 months. You now have a network of

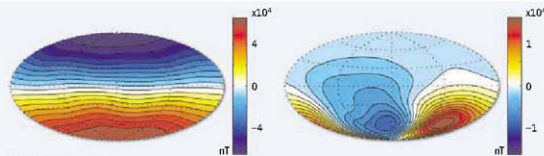
essentially everybody who's funding government science meeting on at least a 3-monthly interval. A real community is now starting.

Q: David King took a very public stance, putting advice into the public domain even when he disagreed with the government. What approach do you favor?

J.B.: The key thing is that if there's an issue, it needs to be raised. The one that I raised very early on in my tenure was the issue of food security, which I felt had been quite seriously neglected, and the related issue of biofuels. In my first speech [as chief scientific adviser], I raised these issues. Very substantial increases in food prices shortly followed and [there was] a very quick reaction by the prime minister, who raised the issue of food security at the G8 Summit the following summer. Some issues are better raised involving the media and the public at large; others are better talking behind the scenes.

Q: On biofuels, your concern was the competition for arable lands?

J.B.: When I first raised [the issue], I made the point that some biofuels were being produced by cutting down rainforests or using permanent grassland, which has a negative effect on greenhouse gas emissions. So you



GEOPHYSICS

Skewed. Uneven heating of a core producing a normal magnetic field (left) concentrates the field (right).

versity of Wisconsin, Madison, draw on magnetic fields locked into lavas as they solidified in Germany and on Tahiti since 780,000 years ago. Five times during a 200,000-year interval, Earth's magnetic field weakened for thousands of years as if it were about to switch its north and south poles, only to return to full strength without reversing. During each such excursion, magnetic field lines that had been pointing in the usual direction—roughly toward the geographic poles—swung around as if one pole were someplace in Eurasia and the other around western Australia.

That pole pattern during ancient excursions has a familiar look, Hoffman and Singer note. Mathematically remove today's powerful, axially aligned dipole field—the sort produced by a bar magnet—from Earth's normal field, and the remaining complex but weak field would skew the pole positions in

Mariners have been navigating by Earth's magnetic field for centuries. Seismologists detected the fluid-iron core that generates the magnetic field a century ago. But geodynamists still struggle to understand exactly how the churning of the core's fluid iron generates the field inside Earth. One secret, according to two papers in this issue of *Science*, may lie in the far slower roiling of the solid rock overlying a planet's core. The

authors draw on magnetic fields long frozen into the rocks of Earth and Mars to understand how motions in the solid rock can shape a planet's magnetic field.

Here on Earth, the frozen fields link the deep-seated magnetic field to plate tectonics at Earth's surface. On page 1800, paleomagnetist Kenneth Hoffman of California Polytechnic State University in San Luis Obispo and geochronologist Brad Singer of the Uni-

COURTESY OF STANLEY ET AL., SCIENCE

don't want to be doing that. I think that the [U.K. government's] Gallagher Report indicates that there's some need for caution on the development of biofuels within the U.K. and Europe. It's a complicated issue. The information that is available to make a comprehensive assessment of the implications of biofuels is quite inadequate.

Q: You have said that the world needs to dramatically increase food production, using less water than is used today. Will the world need to embrace GM technology?

J.B.: Population growth and the increase in wealth implies something like a 50% increase in food demand by 2030. At the same time, the proportion of the population that lives in an urban environment will go up from about 47% to 60%. That means there's going to be some real problems for agriculture. Essentially, about 70% of available freshwater is used by agriculture. There's going to be competition [for water] between urban communities and agriculture relatively close to urban communities. I'm worried about that.

GM is not going to be the only answer. The knowledge of the plant genome is going to be absolutely critical to improving agricultural production. GM is only one of the



British advisory. John Beddington warns that increasing energy, food, and water demands are vital security issues.

techniques that can be used; marker-assisted breeding could be used equally well.

Q: The U.K. government is falling behind its own targets for reducing greenhouse gas emissions. How should it catch up?

J.B.: There's some interesting work that's being done by the government's new Climate Change Committee, which is going to be reporting in December, that is going to answer those questions very specifically. The Energy Technology Institute, funded jointly by industry and government, is looking at operational

scale inputs to a whole series of green engineering technologies to address these problems. The big [initiative], which everybody really needs to be addressing, is CCS [carbon capture and storage]. And that really needs very serious investment.

Q: At U.K. universities, many physics and chemistry departments have closed because of declining student numbers [Science, 12 September, p. 1428]. Should the government intervene to support strategic science subjects?

J.B.: I think it's absolutely critical that we make certain the STEM agenda works—science, technology, engineering, and mathematics are the subjects that we desperately need students to take A-levels [high school finals] in and go on to do degrees. There has been a downward trend [in undergraduate STEM enrollment], but I think it is actually starting to reverse. One area that has been very successful in reversing this [overall] downward trend has been the Ambassador Scheme, in which we've got something of the order of 20,000 scientists and engineers going into schools, talking to students about their lives and the problems they're actually facing. Now our commitment is to expand that.

just that way. Hoffman and Singer infer that this field, called the nonaxial dipole (NAD) field, was there three-quarters of a million years ago. Ever since then, the pair argues, something must have kept the molten iron of the core swirling in the same pattern to generate the NAD field.

The ultimate stable driving force appears to be plate tectonics. Lots of cold oceanic plates have sunk through the mantle to the top of the core beneath Western Australia. That relatively cold material would cool the underlying core fluids, which would sink, superimposing a weaker but persistent circulation on the one generating the main dipole field. Hoffman and Singer suggest that the field-generating circulations are layered, with the main dipole field generated deep within the outer core and the NAD generated near its top.

Dynamo specialists say this paleomagnetic argument indicates that mantle rock influences the magnetic field, as modern observations had hinted. "It's very likely the

mantle does have a role in the core flow," says geophysicist Peter Olson of Johns Hopkins University in Baltimore, Maryland, "but it's not that easy to say one [field] is shallow and the other is coming from deep."

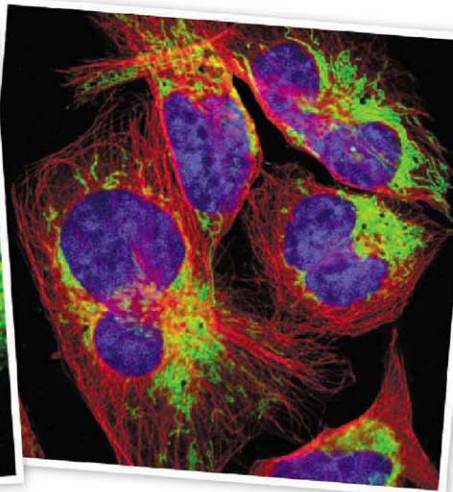
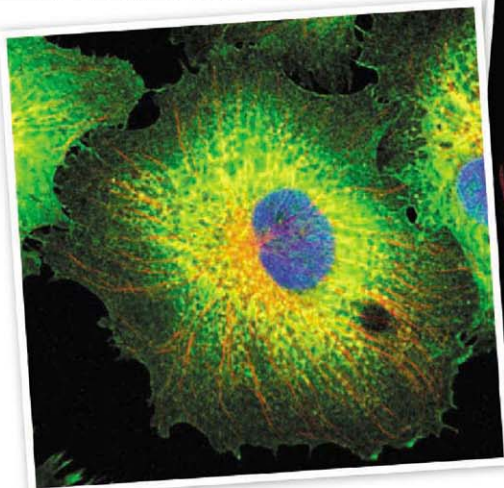
On Mars, the patches of magnetic field detected from orbit froze into the crust more than 4 billion years ago, not long before the dynamo in the martian core died. Oddly, the patches of field lingering in the northern hemisphere are far weaker than those in the southern hemisphere. The planet's crust also differs between hemispheres. It's thin and low-standing in the north but high and thick in the south. Could the two asymmetries be related? On page 1822, dynamo specialist Sabine Stanley of the University of Toronto, Canada, and colleagues consider the possibility.

In a dynamo computer model, Stanley and her colleagues made the bottom of the mantle colder in the southern hemisphere than in the north. That would be the temperature pattern imposed on the core by a mantle

circulating so as to create the crustal asymmetry: hotter mantle rock slowly rising throughout the northern hemisphere in one great plume—thinning the crust by eroding it—and cooler mantle sinking throughout the southern hemisphere. Researchers have suggested several ways such a mantle circulation might have been created, including a supergiant impact (*Science*, 11 April, p. 165). Once the resulting temperature pattern was imposed on the model mantle, it induced a circulation in the molten core that generated a magnetic field, but almost entirely in the south and only weakly in the north.

Creating a lopsided magnetic field is "a significant accomplishment," says planetary physicist David Stevenson of the California Institute of Technology in Pasadena. But proving that early Mars worked that way will require a better record of early magnetic field behavior, he cautions. Understanding long-term interactions between the mantle and the magnetic field will take a lot more work.

—RICHARD A. KERR



Proteomics Ponders Prime Time

Improved technologies for tracking thousands of proteins at once have spawned talk of a full-scale project to reveal all the proteins in each tissue—but the price tag would be daunting

AMSTERDAM, THE NETHERLANDS—He's too polite to come right out and say it, but Amos Bairoch thinks that much of the data generated by proteomics groups over the past decade is junk. Following the completion of the human genome project, proteomics labs set out to survey all the proteins expressed in different cells and tissues, in essence, putting meat on the bone of the genome. Mass spectrometers and other tools turned out gigabytes of data that purported to identify large numbers of proteins and fed them to Bairoch, who heads Swiss-Prot, a massive database that houses the latest findings on proteins of all stripes. Today, most of those data are ignored, Bairoch says, because the readings were too imprecise to make positive identifications. Throughout the years, many casual observers of the field dismissed proteomics as a waste of time and money. "People thought [the technology] was ready 10 years ago. But they didn't see good results and got disenchanted," Bairoch says.

Today, however, Bairoch's databases and others like them are filling up with terabytes

of information that he calls "much better." The upshot: Proteomics is finally coming of age. With the help of better instrumentation and refined techniques, the top proteomics labs can identify and quantify more than 6000 distinct proteins from individual cells and tissues at a time. Now that these labs can cast such a wide net, many proteomics researchers say the time is ripe to undertake a full-scale human proteome project (HPP) to survey the landscape of proteins present in dozens of different human tissues. If successful, such a project would reveal which proteins are actually expressed in different types of cells and tissues, and at what levels, and the network of proteins they communicate with. That knowledge could offer researchers innumerable insights into how organisms convert their genetic blueprint into life and perhaps lead to breakthroughs in biology and medicine. "We are at the point where we can talk about doing this in 8 to 10 years," says Mathias Uhlen, a microbiologist and proteomics expert at the Royal Institute of Technology in Stockholm, Sweden.

It's not just talk. Uhlen and other proteomics leaders gathered here last month to weigh plans for an HPP and to sound out representatives of science funding agencies that would need to pony up the hundreds of millions—if not billions—of dollars needed to pull it off. Most of the responses suggested that tight science budgets make a new megasized international science project unlikely anytime soon. Nevertheless, even without a coordinated international HPP, the field is moving so fast that "it's happening already," says Matthias Mann, a proteomics expert at the Max Planck Institute of Biochemistry in Martinsried, Germany.

Spotted history

Many researchers probably assume an international proteome effort started years ago. The availability of the human genome sequence in 2001 told researchers how many proteins are likely to be out there and the exact sequence of amino acids they should look for. The race was on, amid plenty of hype. "Everyone was interested in proteomes," says Mann.

But there were problems, lots of them. For starters, proteins are chemically far more heterogeneous and complex than DNA and RNA. It was relatively easy for researchers to

COURTESY: UNIKLINIK KLINIKUM KÖLN; UNIKLINIKUM KÖLN

Revealing. Fluorescent antibodies flag the locations of different proteins in cells, offering clues to those whose functions are unknown.

create a single, robust, and standardized sequencing technology to decode the genetic blueprint of humanity. But no single machine could tell researchers everything they wanted to know about proteins. Worse, although each cell contains the same complement of genes, the abundance of different proteins varies widely. One milliliter of blood, for example, contains about 1 picogram of cell-signaling molecules called interleukins and about 10 billion times that amount of a protein called serum albumin. Such plentiful proteins can mask the signals of their rare brethren.

Still, the lure of proteins was undeniable. Whereas genes are life's blueprint, proteins are the bricks and mortar from which it is built. Identify a critical protein in a disease process, and it could serve as a target for a multibillion-dollar drug to fight diabetes or heart disease. Fluctuations in the amounts of some proteins could serve as "biomarkers" to alert doctors to the onset of cancer or Alzheimer's disease. In the early part of this decade, companies flocked to the field, raising and spending hundreds of millions of dollars. But it quickly became clear that the technology was immature. After several years of trudging down blind alleys, most of the companies that were formed to hunt for biomarkers and drug targets were either folded or merged out of existence (see sidebar, p. 1760).

The news wasn't much better in academia. Take an early example from the Human Proteome Organisation (HUPO), which was launched in 2001 to coordinate international proteomics research and bring order to the unruly field. In 2004, HUPO launched its Plasma Proteome Project (PPP) to survey blood proteins and propel the search for candidate biomarkers. HUPO sent identical blood samples to research groups around the globe, each of which conducted its own analysis with its own homegrown version of the technology. "It was a big disaster," says John Yates, a chemist and mass spectrometry (MS) expert at the Scripps Research Institute in San Diego, California. "There was no quality control. Then the data came back, and it was just a mess," he says.

Unfortunately, PPP and other early

efforts raised expectations that they would produce a shortcut for finding novel biomarkers for a wide variety of diseases. "The plasma proteome [project] made the search for biomarkers look like a slam dunk," says Jan Schnitzer, who directs the vascular biology and angiogenesis program at the Sidney Kimmel Cancer Center in San Diego. "But it hasn't delivered." That failure and the failure of proteomics as a whole to deliver on its promise, Uhlen adds, "is a history which is still haunting us."

HUPO has since promoted uniform standards for everything from how to collect and process blood and tissue samples to the proper methodologies for screening them and analyzing the data. And PPP is now taking a more targeted approach to discovering proteins.

The standards have helped, but they haven't solved all the problems. A study last year compared the ability of 87 different labs to use MS to identify correctly 12 different proteins spiked into an *Escherichia coli* sample. No lab got them all, and only one correctly identified 10 of the 12, says Thomas Nilsson, a proteomics researcher who splits his time between Göteborg University in Sweden and McGill University in Montreal, Canada. In a follow-on study completed this year, only six of 24 labs correctly identified 20 spiked proteins. "That again is quite depressing," Nilsson says. "So what are the chances [for

success] of high-throughput proteomics as a distributed effort?" Nilsson asked attendees in Amsterdam.

Perhaps surprisingly, Nilsson says he thinks they are decent. This year's study, he explains, shows that most errors in MS-based analyses arise not because the technology can't spot the proteins researchers are looking for but because software programs often misidentify them.

A big part of the problem, says John Bergeron, a proteomics expert at McGill University, rests with simple statistics. To identify proteins using MS, researchers first

chop a sample of proteins into smaller fragments called peptides. Those peptides are fed into a mass spectrometer, which ionizes them and shoots them through a chamber. The time it takes for the ions to "fly" through the chamber reveals the atomic weight of the peptides, which in turn reveals their identities. Computer programs then compare them with a full list of the organism's genes, which code for those peptides and their proteins. If a peptide matches the protein code in only one gene, it is a hit and it is a unique identifier of the protein.

The problem is that not all peptides are successfully ionized in each experiment, so some don't enter the chamber. Even if the same lab runs a sample of proteins through the machine twice, Bergeron says, 33% of the proteins identified will appear to be different between the two runs. To minimize such sampling error, MS labs now typically

"The biology community at large has to show they really need this. If they can't, why should they fund this?"

—AMOS BAIRICH,
SWISS-PROT



Pacesetter. Thanks to better mass spectrometers and software, researchers such as Matthias Mann (inset) can now identify thousands of proteins in a single experiment.

run samples through their machines as many as 10 times. Today, MS groups also look for more than one unique peptide to confirm the identity of a protein. Those changes, together with other emerging standards, show that "these are problems that can be addressed," Schnitzer says.

A new approach

Such successes are also convincing proteomics leaders that the technology is mature enough to go after a full-scale HPP. Although details remain in flux, the generally agreed-upon plan is to identify one protein for each of the estimated 20,400 human genes. Bairoch reported at the meeting last month that Swiss-Prot has logged what is currently known about each gene, such as the primary proteins a particular gene produces and their function. Proteins for about

half of the genes have never been seen, Bairoch stated.

There are far more proteins than genes, because proteins can be spliced together from multiple genes, and once synthesized, they can later be cut down in size or modified with other chemical groups. Trying to find all those variants in all tissues is a task that will likely take decades, Uhlen says. Sticking to one protein for each gene provides a defined endpoint to the project and would create a "backbone" of all human proteins that can be continually fleshed out.

Another possible goal is to create one antibody for every protein in HPP. Because antibodies typically bind to one target and nothing else, researchers can use them to fish out proteins of interest and track their locations in cells and tissues. That would offer clues to the functions of the thousands

of proteins for which little is known. Uhlen and colleagues in Sweden launched just such a global antibody project in 2005. And in Amsterdam, Uhlen reported that the catalog now contains more than 6000 antibodies against distinct human proteins, more than one-quarter of the complete set. At the current rate of new antibody production, Uhlen says his team will finish the task in 2014. More money, he says, would undoubtedly speed the effort.

A third project would track which proteins "talk" to one another. To find a protein's partners, researchers create thousands of identical cell lines and insert into each one a chemical tag linked to a different protein. They can use the tag to pull that protein out of the cell at a specific point in its life cycle, along with any other proteins, bits of RNA or DNA, or a metabolite that it is

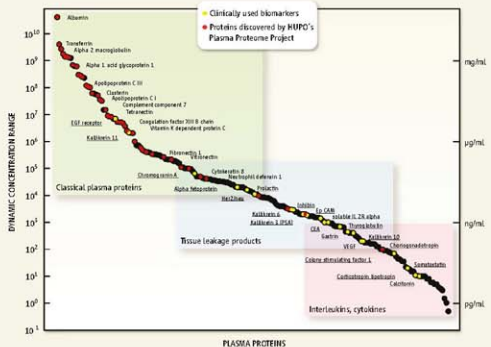
Will Biomarkers Take Off at Last?

One much-heralded application of proteomics—detecting proteins that are markers for specific diseases—has long been a dream deferred. "It has been extremely difficult to find those proteins that are biomarkers," says Ruedi Aebersold, a proteomics expert at the Swiss Federal Institute of Technology in Zurich, Switzerland, and the Institute for Systems Biology in Seattle, Washington. But after years of disappointments, proteomics researchers say they're cautiously optimistic.

When proteomics caught fire earlier this decade, scientists hoped that mass spectrometry (MS) and other technologies would help them sift through the thousands of proteins in blood and other body fluids to identify a rare protein that indicated the presence of a disease. Researchers could then use these biomarkers to spot diseases in their formative, treatable stages. But the demise of several companies, such as GenePro and Large Scale Biology, that jumped into the field revealed that nailing down biomarkers is harder than it sounds.

One problem is that blood—the most common hunting ground—is difficult to work with. Levels of different proteins in blood vary by 10 orders of magnitude, and the abundant proteins often mask the presence of rare ones. Unfortunately, mass spectrometry, the best tool for casting a wide net to search for proteins, hasn't been sensitive enough to spot the rare ones. "Most clinically used biomarkers are at nanogram [per milliliter] levels or below," Aebersold says. At the meeting, Aebersold reported a new strategy for targeting protein fragments called N-linked glycopeptides, which commonly make up cell-surface receptors and thus are more likely to be shed into the blood. This targeting allowed Aebersold's team to spot proteins down to nanogram-per-milliliter levels and thereby track them to look for possible links to diseases. Aebersold says he's hopeful that similar, more focused, studies will improve prospects for the biomarker hunters.

Better instrumentation won't solve all the problems. Techniques such as MS that survey thousands of different compounds inevitably



Needles in a haystack. The abundance of different proteins in blood varies by more than 10 orders of magnitude. Most commercially used biomarkers (yellow dots) are present in only minute quantities in blood, below the level at which most proteins are detected (red dots).

turn up false positives: proteins that change their abundance in lock-step with a disease just by chance. That means candidate biomarkers must be validated through clinical trials, which can cost tens of millions of dollars—and most of them fail. "To be accepted by [regulatory] agencies, it's almost as costly as developing a new drug," says Denis Hochstrasser, the director of laboratory medicine at Geneva University Hospital in Switzerland. Because diagnostics companies, unlike drugmakers, typically can't charge lofty premiums for their new tests, they have less incentive to develop biomarker tests. Michael Snyder, a proteomics expert and cell biologist at Yale University, says that despite these challenges, he's hopeful that improving proteomics technologies will generate novel biomarkers—"just not on the same time frame as people thought."

—R.F.S.

bound to. Bioinformatics experts can then weave together the partners for each protein to construct a complete communication network of the proteins in the cell.

Such protein-interaction networks have been worked out in exquisite detail in yeast and other organisms. But it has been hard to insert the chemical tags reliably into human cell lines. Over the past decade, however, researchers around the globe have shown that different lentiviruses readily insert tagged proteins into a wide variety of human cells. At the meeting, Jack Greenblatt of the University of Toronto in Canada said he has proposed a project to insert one tagged protein for each of the 20,400 genes, the first step to a complete human proteome interaction map. The project is now under review by Genome Canada, the country's national genome sciences funding agency. Greenblatt adds that working with human cell lines isn't perfect, because these lines are typically made up of non-normal cells that have been immortalized. His group is also performing related studies in mice, which can be grown into adult animals, and the interaction networks can be compared with those found in the human cell lines. Other projects could be added to HPP as funding permits. They could include a catalog of all the modified proteins, such as splice variants and phosphorylated proteins, Bergeron says.

Finding the money

How much will it take to complete the wish list? Opinions vary, but somewhere in the neighborhood of \$1 billion is a common guess. Michael Snyder, a yeast biologist at Yale University, thinks that's too little. "This is going to require a bigger budget than that," he says.

Whatever the projection, it was enough to make those with the money blanch. Funding agencies around the world are already collectively spending hundreds of millions of dollars on proteomics technologies and centers. They're also already committed to several international big biology projects such as the International HapMap, the International Cancer Genome Consortium, and the Knockout Mouse Consortium, which are putting the squeeze on tight budgets. "From a funding viewpoint from the U.S. context, now is not the right time," says Sudhir Srivastava, who directs proteomics initiatives at the U.S. National Cancer Institute in Rockville, Maryland. "If this was 5 years ago when the NIH [National Institutes of Health] budget was doubling..." Srivastava trails off.

Still, Uhlen and others say they are hopeful that funding agencies will keep the

field moving quickly. "We don't have to have \$1 billion from the start," Uhlen says. "With the Human Genome Project, it took 5 years for the funding agencies to put serious money into it. I don't think we should expect funding agencies to jump on board until we have proven the technology."

To do that and make the cost more palatable, HUPO leaders are mulling a pilot project to catalog all the proteins produced by chromosome 21, the smallest human chromosome, which has 195 genes. Although the cost of such a project isn't known, "I think there almost certainly would be interest," says Roderick McInnes, director of the Institute of Genetics at the Canadian Institutes of Health Research in Ottawa.

At the meeting, proteomics expert Young-Ki Paik of Yonsei University in Seoul, South Korea, said the Korean government is considering funding a similar proposal for a Korean-based pilot project on chromosome 13, the second-smallest human chromosome, with 319 genes. Paik says he and his colleagues have proposed a 10-year, \$500 million initiative that is currently being considered by the Korean Parliament. A decision is expected in October. If it is funded, Bergeron says it will be a major boost to the field and could help catapult Korea into the forefront of proteomics.

Some researchers are skeptical of going chromosome by chromosome, however. "In gene sequencing, that approach worked," Bairoch says. "You could separate out the work by chromosome. But it doesn't make sense for proteins. There is no [body] fluid or [tissue] sample organized by chromosome." Ruedi Aebersold, an MS expert with a joint appointment at ETH Zurich and the Institute for Systems Biology in Seattle, Washington, agrees. "I'm not a big fan of going chromosome by chromosome," he says. MS machines, he notes, identify whatever proteins show up regardless of the chromosomes they came from.

Whatever path they take to an HPP, proteomics leaders will need to find true believers beyond those already in the flock. "The biology community at large has to show they really need this," Bairoch says. "If they can't, why should they fund this?" Uhlen, Bergeron, and other HUPO leaders



"We are at the point where we can talk about doing this in 8 to 10 years."

—MATTIAS UHLEN, ROYAL INSTITUTE OF TECHNOLOGY

agree. And they argue that current demonstrations of the technology are starting to build the case.

At the Amsterdam meeting, for example, Mann reported that recent advances in instrumentation and software have enabled his group to identify the complete yeast proteome in one shot—in just a few days. That feat took months of painstaking effort when it was first accomplished by traditional methods 5 years ago. Mann also described the use of a technique his team first reported last year to monitor changes in the yeast proteome, including levels of individual proteins, between two different states. In one example, Mann's team compared yeast cells with a diploid (double) set of chromosomes to cells with the haploid (single) set undergoing sexual reproduction. The study quantified for the first time the suite of proteins that orchestrate sexual reproduction in yeast. Mann says the technique opens the door to studying proteome-wide differences between healthy and diseased cells, developing and mature cells, and stem cells and differentiated cells. "There is no end to what you can compare," Mann says. "Every lab can ask these questions."

In an another study, Uhlen reported using his antibodies to track global protein expression in human cells. He and his colleagues have shown that fewer than 1% of all proteins are expressed in only one tissue. That implies, he says, that tissues are differentiated "by precise regulation of protein levels in space and time, not by turning expression on and off." Aebersold also reported that his lab has devised a scheme for detecting proteins expressed at the level of just a single copy per cell.

"These are unbelievable advances, and they show we can take on the full human proteome project immediately," Bergeron says. Not everyone has turned that corner, but Bergeron and others say that they are confident that time is coming soon. As Pierre LeGrain, director of life sciences at the French Commissariat à l'Energie Atomique in Gif-sur-Yvette, sums it up: "Most of us feel the human proteome project is going to happen, though we don't know how."

—ROBERT F. SERVICE

ELECTION 2008

Scientists Strive for a Seat at the Table of Each Campaign

When it comes to soliciting scientific advice, Barack Obama welcomes a cast of thousands, whereas John McCain plays it close to the vest

Harold Varmus has met Senator Barack Obama only once. But he's convinced that the Democratic presidential nominee "understands the important role that science must play in tackling the problems we face as a society." To prove it, the president of Memorial Sloan-Kettering Cancer Center in New York City points to the candidate's promise of "sustained and predictable increases in research funding" at the major federal science agencies.

It's no surprise that the politically active Varmus, the 1989 medicine Nobel laureate and former director of the U.S. National Institutes of Health (NIH), is familiar with Obama's statements on funding basic research: He helped write many of them as chair of a 40-plus-member committee of prominent researchers and educators who are advising the freshman senator from Illinois on science. The panel prepared the candidate's 6000-word response last month to 14 questions posed by a coalition of scientific organizations called Science Debate 2008 (ScienceDebate2008.org). Varmus won't say how much the answers were altered by campaign officials but allows that "we're very pleased with it. His commitment to science is absolutely apparent."

Last week, Obama's Republican opponent, Senator John McCain (AZ), provided equally lengthy answers to the same set of questions. Douglas Holtz-Eakin, who serves as the candidate's point man on many domestic policy issues, including science, health, energy, and the environment, says McCain has contacted experts on issues such as climate, space, and "science in general" but has "no formal structure" for soliciting advice. An economist and former head of the Congressional Budget Office under President George W. Bush, Holtz-Eakin says McCain relies instead on the knowledge acquired during

Online

sciencemag.org

Podcast interview with the author of this article.



Science and the 2008 Campaign

his 26 years in Congress, including 6 years as chair of the Senate Commerce, Science, and Transportation Committee.

The way the answers were prepared reflects the different management styles of the two campaigns. "Obama has thousands of advisers, and McCain has two guys and a dog," cracks one academic lobbyist who requested anonymity because his organization tries to maintain ties with both camps.

The answers themselves—on research funding, science education, climate change, energy, space exploration, and other issues—reflect different political philosophies. Obama tends to assign government a larger role in tackling those problems—a \$150 billion plan for energy independence, for example, and an \$18 billion plan to improve education. McCain, in contrast, combines his \$30 billion clean-coal program with talk about the need to curb spending and rely on the private sector.

For many U.S. academic researchers, presidential politics comes down to two big issues: getting more money for science and having a seat at the table. The first requires agreement between the president and Congress, however, and any promise to increase research spending could easily be derailed by the Iraq war, an ailing economy, and rising health care and

energy costs. That puts a premium on the second issue, namely, the appointment of people who will make the key decisions in the next Administration.

Indeed, three independent panels stuffed with science winners have recently issued reports "emphasizing the importance of choosing an assistant to the president for science and technology soon after the election. They say that person, who would also head the Office of Science and Technology Policy (OSTP), should be part of the president's inner circle and play a major role in vetting appointments to dozens of other key science positions throughout the government.

"We had drafted white papers on several issues, but the presidents [of the three academies] worried that nobody would pay attention to them," says E. William Colglazier, executive officer of the U.S. National Academy of Sciences, which joined with the engineering academy and the Institute of Medicine in issuing a report last week on the appointment process. "They felt it was more important that the next president get very good people into key positions." Working backward, scientists reason that the more interaction with a candidate before election day, the greater the chance that he will act quickly and fill those posts with highly qualified people.

Since declaring his candidacy in February 2007, Obama has welcomed those interactions. He has solicited the views of troves of experts and created a vast network of advisers. "They didn't ask us to take a blood oath," says Varmus, who endorsed Obama with the Democratic nomination still hanging in the

"The reports were done by the Woodrow Wilson International Center for Scholars (OSP2.0.CriticalUpgrade.com); the Center for the Study of the Presidency (PresidentialPersonnelandAdvisoryRequirements.org); and the three national academies (ScienceandTechnologyforAmerica'sProgress.org), ensuring the best Presidential Appointments, at nationalacademies.org).



Many voices. Harold Varmus (far left) and other leaders joined Barack Obama at a June economic roundtable at Carnegie Mellon University.

CREDIT: CARNEGIE MELLON UNIVERSITY

balance. But he says "it's a reasonable assumption" that most of the advisers also support his candidacy.

Varmus's panel, which includes medicine Nobel Peter Agre and physics Nobel Leon Lederman, is one of 20 or so advisory bodies. (The Obama campaign declined to provide a number.) Paul Kaminski, a top Pentagon official during the Clinton Administration, is heading up an eight-person group on defense science that is examining work-force, training, and acquisition issues. He'll also be representing Obama next month at a National Academy of Engineering forum on grand challenges, opposite Carly Fiorina, the former CEO of Hewlett-Packard who was once on McCain's list of possible running mates. There's another Obama group on science education, and the membership is overlapping. Kaminski recently joined the science panel, for example, and Lederman also serves on a small group examining science education.

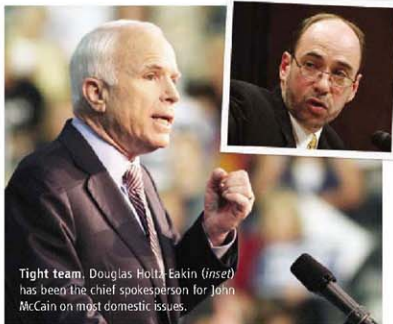
With regard to scientific input in a McCain Administration, Holtz-Eakin promises that McCain will be vigilant in ending what critics have called the Bush Administration's war on science. "He'll restore credibility and transparency" to the process, says Holtz-Eakin, in part by filling all six statutory positions at OSTP. Still, Holtz-Eakin knows that he's addressing a skeptical audience. "You can't convince people that you'll make sure they have access. You have to demonstrate it," he told *Science*.

Convened this summer, Obama's science group has held weekly teleconferences to field questions from the campaign staff and inject into the campaign issues that it feels are important. In preparing answers to Science Debate's 14 questions, the panel's most visible product, members sifted through Obama's past statements, added their own perspectives, and delivered answers to Jason Furman, Obama's director of economic policy, via his deputy, Larry Strickling.

The panel's fingerprints are evident in the nuanced responses that Obama offers. To a question about how basic research would fare in a competition for scarce funds, for example, Obama discusses the declining success rate among applicants for NIH grants, the resulting pressure on young scientists, and the erosion of the agency's buying power after a succession of flat budgets that followed a 6-year doubling from 1998 to 2003. In such an environment, he adds, scientists are less inclined to take risks.

"This situation is unacceptable," he declares, offering as the solution a 10-year, across-the-board budget doubling in the physical and life sciences, mathematics, and engineering.

McCain is less sanguine than Obama about the likelihood of large increases. "I have supported increased funding at DOE [Department of Energy], NSF [National Science Foundation], and NIH for years," he notes in his Science Debate reply, "and will continue to do so." But he warns that "with spending constraints, it will be more important than ever to ensure that we are maximizing our investments in basic research." And his answer omits mention of any numerical goal. In an interview last month on National Public Radio, Holtz-Eakin



Tight team: Douglas Holtz-Eakin (inset) has been the chief spokesperson for John McCain on most domestic issues.

said any call for doubling science agency budgets is "a nice, fun number... that doesn't reflect a balancing of political priorities."

In fact, it's hard to pin down either candidate on how quickly he would like to increase federal funding for basic research. Making a video appearance this month during a cancer research telethon, Obama promised to double the budget of NIH, including the National Cancer Institute, in 5 years. That's twice the rate described in his answers to Science Debate, which came out in August and have become the mantra for campaign surrogates. He also supports the 2007 America COMPETES Act (ACA), which is silent on NIH but which would put NSF and DOE's Office of Science on a 7-year doubling track.

As it happens, those figures are in line with historical trends. Between 1962 and 2003, for example, the NIH budget doubled roughly every 8 years, in current dollars. NSF has seen its budget double every decade for the period from 1970 to 2000.

A statement on McCain's Web site also promises to "fully fund" the provisions of the

COMPETES Act, which authorizes spending levels that have not been met in subsequent appropriations bills. Holtz-Eakin told *Science* that McCain "is on the record as supporting ACA" and that, if elected, his 2010 budget would reflect those targets in the physical sciences. Taking a jab at Obama's expansive promises for increased spending in research and other domestic areas, Representative Vern Ehlers (R-MT) predicts the U.S. research enterprise will be better off under a McCain Administration, despite its more modest promises, because "he's more likely to find the money." But Ehlers, one of three physics Ph.D.s in Congress and a staunch supporter of science, admits that McCain hasn't sought his

advice on the topic. (His colleague, Representative Rush Holt (D-NJ), has spoken for Obama, although during a recent interview with *Science* he deferred several questions to the campaign staff.)

Obama's aides and outside advisers play down the discrepancies in Obama's statements on NIH doubling while at the same time perpetuating them. Domestic policy director Neera Tanden, who joined the campaign this summer after many years advising Senator Hillary Clinton (D-NY) on health-care issues, says a 5-year doubling of the NIH budget "is the right thing to do" and that it is needed to keep pace with the rapid advances in the field. Tanden also says the disruptions caused by a stagnant NIH budget after the previous doubling aren't inevitable. "There's no reason to assume you would have another crash landing," she says.

Gilbert Omenn, a professor of medicine and public health at the University of Michigan, Ann Arbor, and a former president of AAAS (which publishes *Science*) who serves on Obama's science advisory panel, acknowledges that the different timetables "are very awkward" and that the candidate's promises "add up to a lot of commitments." But he's confident that Obama "will be able to figure out the best combination of variables to allow for a sustained investment."

In the end, of course, promises are only that. "Remember, it's a campaign, not governance," notes Lederman when asked if his group expects to have an impact on Obama's education policies if he takes office in January. A seat at the table may be a better bet, says Kaminski. "I would expect some of [his defense advisers] to take key positions in his Administration." That is, if they turn out to have bet on the winning candidate.

—JEFFREY MERVIS

AGING

Searching for the Secrets Of the Super Old

More and more people are living past 110. Can they show us all how to age gracefully?

They were born when the years still started with "18." They survived global traumas such as World War I, World War II, and the Great Depression. They didn't succumb to pandemic flu, polio, AIDS, Alzheimer's disease, or clogged arteries. Supercentenarians, or people who've survived to at least age 110, are longevity champions.

Living to 100 is unlikely enough. According to one estimate, about seven in 1000 people reach the century milestone. And at that age, the odds of surviving even one more year are only 50–50, says James Vaupel, director of the Max Planck Institute for Demographic Research in Rostock, Germany. Making it from 100 to 110 "is like tossing heads 10 times in a row."

Researchers are keen to investigate these 19th century holdovers. "If we want to better understand the determinants of longevity, we have to look at the oldest old," says biodemographer Jean-Marie Robine of INSERM's demography institute in Montpellier, France. With Vaupel, he has recently compiled a demographic database of verified supercentenarians from the industrialized countries.

Two other projects, led by researchers on the opposite coasts of the United States, hope to pin down the traits of these survivors by surveying their genomes for longevity-promoting DNA sequences and by autopsying them when they finally die. Ultimately, work on supercentenarians could uncover "a unique [genetic] variation that explains their longevity that can be the subject of drug development," says molecular geneticist Nir Barzilai of Albert Einstein College of Medicine in New York City. Such a discovery might not stretch human life span, but it could make our final years less grueling, suggests Barzilai.

Yet studying supercentenarians is no easy task. Finding these one-in-a-million people is hard enough, and validating their ages can require that researchers become detectives or hire ones.

Come on, how old are you really?

Figures on the number of supercentenarians are shaky. The 2000 U.S. census claimed a total of 1400 living in the country. That number is much too high, says geriatrician Thomas

Perls of Boston University School of Medicine, head of the New England Centenarian Study and its new National Institutes of Health-funded spinoff, the New England Supercenarian Study. Researchers suspect that some of the oldest included in the tally had already died and that others—or their relatives—were lying about their ages. Drawing on Medicare enrollment figures, two U.S. government actuaries put the number of supercentenarians in the year 2000 at a mere 105. And in 2002, 139 people claiming to be at least 110 were receiving Social Security payments.

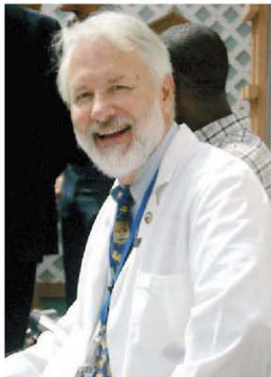
"Claiming" is a key word. A crucial part of studying supercentenarians is proving that they were or are their stated age. No biochemical test or medical exam can peg how old somebody is. So researchers often turn to Robert Young of Atlanta, Georgia, a self-taught documents guru who confirms the ages of the world's oldest people for *Guinness World Records*. Young comes across like a veteran insurance adjuster who's seen all the scams. To weed out pretenders,

he requires three types of verification: proof of birth, preferably a birth certificate; proof of death, if the person is no longer alive; and "continuity" documentation, such as a driver's license or marriage certificate, that shows that the putative supercentenarian is the person listed in the birth record. If candidates or their families can't provide corroboration, Young sleuths through census rolls, school and military records, genealogies, and other types of paperwork.

Using these methods, an organization called the Gerontology Research Group verifies the ages of living supercentenarians and posts a list online (www.grg.org). Young is senior claims examiner for the group, which is headed by L. Stephen Coles of the University of California, Los Angeles, an ob-gyn and computer scientist by training. As of last week, the roster included 10 men and 68 women from 12 countries, ranging up to 115 years old. For reasons that remain murky, most supercentenarians are women. Moreover, of the oldest people ever documented, the majority have been women, including the record-holder Jeanne Louise Calment of France, who died in 1997 at the age of 122.

To obtain a more complete count of supercentenarians for demographic analyses, Vaupel, Robine, and colleagues have dug into national archives, including the records of the U.S. Social Security Administration, to compile lists of candidates in 15 industrialized countries. A team of age checkers then vetted each case. In all, the new International Database on Longevity caches information on nearly 1000 supercentenarians from the past 50 years, although not every country's records span this entire range. The researchers plan to publish a monograph on the database later this year.

But that still won't be the final word. A



Cutting for clues. L. Stephen Coles leads a group that has performed most of the autopsies on supercentenarians.

PHOTOS (TOP LEFT TO RIGHT) COURTESY OF GERONTOLOGY RESEARCH GROUP; (BOTTOM) COURTESY OF L. S. COLES

Turn of the century. The world's oldest living person is 115-year-old Edna Parker (right). Daniel Guzman (left), reached 111 before dying earlier this year.

lack of good records in developing nations means that researchers still know little about the numbers of supercentenarians worldwide, says demographer Bertrand Desjardins of the University of Montreal in Canada: "It's anyone's guess how many supercentenarians are living in China."

How to grow old in style

Scientists have gotten a few hints about what keeps centenarians alive for so long—genes associated with a beneficial lipid profile, for example (*Science*, 17 October 2003, p. 373)—but they're just beginning their search for the sources of supercentenarian longevity. Two years ago, Perls and colleagues published the first health survey on these so-called supers, reporting on 32 people between the ages of 110 and 119. "I think it's incredible how well off they are," says Perls. Although almost half of the supers had osteoporosis and almost 90% had cataracts, 41% of them either lived on their own or required only minimal help with tasks such as preparing food, dressing, and bathing. Cardiovascular disease, the leading killer in developed countries, was rare among supercentenarians—only 6% had suffered heart attacks and 13% reported strokes. Diabetes and Parkinson's disease were also uncommon in the group, striking only 3% of the subjects each. Like centenarians, supercentenarians seem to be good at putting off the day when they become disabled, says Perls.

The superseniors deviate from the norm not just in how long they live but in how they die, says Coles, who arranges autopsies of the oldest old as part of his work with the recently established Supercentenarian Research Foundation. Only nine supercentenarians have undergone postmortems—Calment, for example, never agreed to one—and Coles and colleagues have performed six of these procedures, including one earlier this year in Cali, Colombia, on a man who died at age 111.

Coles argues, based on these autopsies, that supers aren't perishing from the typical scourges of old age, such as cancer, heart disease, stroke, and Alzheimer's disease. What kills most of them, he says, is a condition, extremely rare among younger people, called senile cardiac TTR amyloidosis. TTR is a protein that cradles the thyroid hormone thyroxine and whisks it around the body. In TTR amyloidosis, the protein amasses in and clogs blood vessels, forcing the heart to work harder and eventually fail. "The same thing that hap-

pens in the pipes of an old house happens in your blood vessels," says Coles.

Perls and colleagues have also shown that extreme survival runs in supercentenarians' families. Repeating an analysis they did earlier for centenarians, the researchers last year analyzed life spans of the siblings and parents of supercentenarians from the United States. The team compared the relatives' longevity with that of people born in the same year. Brothers of supers gained about 12 to 14 years over their contemporaries, whereas sisters outlasted their counterparts by about 8 to 10 years. A family connection doesn't mean that only genes are responsible for supercentenarians' great age, Perls cautions. Everything from diet to exercise habits can also run in families—the analysis can't distinguish between genetic and environmental factors.

But Perls's current work might. He and his colleagues have collected blood samples from 130 authenticated supercentenarians and have sequenced DNA from 100 of them. As early as this fall, the team could be ready to submit a paper on gene variants that might be stretching supercentenarians' lives, he says. Moreover, because the research team also has data on the supers' past health and lifestyles, it might be able to statistically tease apart environmental and genetic influences on the oldest's life spans.

The Supercentenarian Research Foundation has similar ambitions. In addition to the autopsies this nonprofit group of doctors and researchers has conducted, Coles and his colleagues have obtained a few blood samples and plan to start collecting more next year. However, the effort, which is operating on donations, won't have enough money to sequence DNA from the samples. They will go into the freezer, but Coles says the shrinking costs of sequencing technology should soon make reading the DNA affordable.

The two projects will be sharing Young's age-checking services but nothing else. Perls says he declined to collaborate with Coles's group in part because some of its members are involved in so-called antiaging medicine, whose practitioners claim to be able to alleviate time's ravages with treatments such as injections of human growth hormone (HGH) (*Science*, 8 February 2002, p. 1032). The

rationale is that the hormone's blood levels normally dwindle as we age. But Perls has blasted this off-label use of the hormone—it's only approved for children with stunted growth and adults with pituitary tumors or other rare conditions—as not only unproven and potentially unsafe but also illegal in the United States.

Working quietly outside that fray, Vaupel and colleagues plan to use their new database to answer a question that's been nagging



Saved by a SNP? Tom Perls (right) and colleagues are scanning DNA from people like 110-year-old Mary Marques for longevity clues.

demographers and actuaries: Do the odds of dying in a given year, which rise relentlessly for most of adult life, taper off in the most senior seniors? Demographers want to determine whether the death rate stabilizes so they can test their models of mortality, whereas actuaries need the answer to help governments refine budgets for health care and pensions. If mortality does peak or even begin to decline in very old age, it could mean that people who live past 110 really are super, stronger than the rest of us, Vaupel says.

If centenarians are any guide, researchers will find that supercentenarians have varying backgrounds, lifestyles, and genetic profiles. But as Robine notes, they share one factor: luck. Calment provides a prime example. She outlived her husband, daughter, and grandson. They died from non-aging-related causes—the husband from food poisoning, the daughter from pneumonia, and the grandson in a car accident. So if you hope to reach the big 110, keep a rabbit's foot handy.

—MITCH LESLIE

2008 Visualization Challenge



THE ILLUSTRATION ON THE COVER OF THIS WEEK'S ISSUE OF *SCIENCE* IS A MERGER of science and art, with a good helping of whimsy. Turn to page 1772, and you will see that it is part of a larger illustration depicting elements of the natural world, put together to resemble the Mad Hatter's tea party in Lewis Carroll's *Alice in Wonderland*. It's a magnet for attracting young children into the world of science, a quality that helped it win the first-place award for informational graphics in this year's International Science & Engineering Visualization Challenge.

Online sciencemag.org

Slideshow and podcast interview with finalist judge Alisa Machalek.

For the past 6 years, *Science* and the U.S. National Science Foundation (NSF) have cosponsored annual challenges to encourage cutting-edge efforts to visualize scientific data. We have been supporting these competitions because we firmly believe that bringing data to life visually will be increasingly important in a world in which images, from traditional media to YouTube, are a primary means of communication. New ways of conveying scientific data will be essential not only for increasing public understanding of science and engineering but also for improving communication across scientific disciplines.

This year, we received 181 entries from 20 U.S. states and the District of Columbia and 20 countries. A committee of staff members from *Science* and NSF screened the entries, and an outside panel of experts in scientific visualization reviewed the finalists and selected the winners. The winning entries appear on the following pages.

We encourage you to submit applications for next year's challenge, details of which will be available at www.nsf.gov/news/special_reports/scivis/index.jsp, and to join us in celebrating this year's winners.

Susan Mason of NSF organized this year's challenge. Rachel Zerkowitz of *Science*'s news staff wrote the text that accompanies the images in this special section, and Martyn Green and Tara Marathe put together a special Web presentation at www.sciencemag.org/vis2008.

JEFF NESBIT, DIRECTOR, OFFICE OF LEGISLATIVE AND PUBLIC AFFAIRS, NSF
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ROBERT PATTERSON

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Applications
University of Illinois, Urbana-Champaign





Photography

FIRST PLACE

THE GLASS FOREST

Mario De Stefano, The Second University of Naples

DIATOMS ARE TINY CREATURES, BUT THEY PLAY A BIG ROLE IN CREATING BREATHABLE air; they produce as much as 40% of the world's oxygen. They can also possess an ethereal beauty, as the winning entry, "The Glass Forest" by Mario De Stefano of The Second University of Naples, Italy, shows. De Stefano used a scanning electron microscope to capture these images of the diatom *Licmophora ehrenbergii* from the Mediterranean Sea off the coast of Italy.

The title refers to the fact that diatoms are unique in using silica to build their cell walls and to the interactions between the diatom and its host, which echo the interplay of a forest. Each green, triangle-shaped diatom measures about 30 micrometers across. There are about 100,000 species of diatoms, the largest of which can reach up to 2 millimeters in length.

The micrograph shows *L. ehrenbergii* clinging to the marine invertebrate *Eudendrium racemosum*, in brown. De Stefano intended the image to depict the complex interactions that occur among organisms on the microscopic scale. "This is the study of a community, ... the same community as you would find in a rainforest."

Panel of finalist judges member Malvina Martin praises "The Glass Forest" for its arresting beauty: "This is an invisible piece of our world that plays such an important role. Everyone was pretty awed by that."

HONORABLE MENTION

STRING VIBRATIONS

Andrew Davidhazy,
Rochester Institute of Technology

A TWIST OF THE FINGERS SENDS A STRING INTO a feverish dance. Photographer Andrew Davidhazy of the Rochester Institute of Technology in New York set out to photograph that dynamic by attaching a tiny motor to a cotton string. But he got overzealous in powering up the motor, forcing an atypical torque in the string. "I happened to overspin the string and all of a sudden, the picture was more exciting," he says. Davidhazy used a Canon digital camera to document the movement. The total exposure time for "String Vibrations" was about 2 seconds, during which the string spun some 10 to 20 times, the photographer says.

HONORABLE MENTION

SQUID SUCKERS: THE LITTLE MONSTERS THAT FEED THE BEAST

Jessica D. Schiffman and Caroline L. Schauer, Drexel University



CRUNCH. THE SATISFYING SOUND OF A CRUSHED COCKROACH COMES from the destruction of its chitin-based exoskeleton. The white, fang-like circles in this electron micrograph of squid suckers are also chitin, but they are not so easily crushed. Their scant 400-micrometer diameter belies the true power of the suckers. A squid uses them to latch onto prey and force the unfortunate creature to its beak, where it is readily slurped down. "They're just tiny things, but they really keep the beast alive," says Jessica Schiffman, a doctoral student in material science engineering at Drexel University in Philadelphia, Pennsylvania. She compiled the image while researching chitin properties in the lab of Caroline Schauer. The iconic film *Little Shop of Horrors* inspired the color scheme, she says.



HONORABLE MENTION

POLYMAZING

Ye Jin Eun and Douglas B. Weibel,
University of Wisconsin, Madison

THE COMBINATION OF POLYETHYLENE GLYCOL (PEG) AND polydimethylsiloxane creates what Ye Jin "Jenna" Eun calls a "sandwich of polymers." But when the University of Wisconsin, Madison, doctoral student added water to her creation, it was clear the union of these polymers didn't emulate peanut butter and jelly's happy marriage. PEG wants to expand when it encounters water, but the stiffer polyethylene copolymer won't permit it. So PEG stretches vertically instead, creating the hills and valleys seen here. The contortions make the polymer combo unusable for the original purpose: mounting cell samples. But Eun, who works under the direction of biochemist Douglas Weibel, says the result of the failed experiment was so beautiful, she photographed the image. She used a Zeiss stereoscope and a Nikon CCD camera.

