

SCIENCE NEWS

THE WEEKLY NEWSMAGAZINE OF SCIENCE

AUGUST 11, 2007 PAGES 81-96 VOL. 172, NO. 6

bones linked to blood sugar
wild ferrets thriving
cancer-vaccine progress?
perils of plastics

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saving saws



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Cover Sawfish, massive marine predators, almost went extinct, but they're now about to receive protection under an international treaty. New research is revealing the life history of these relatives of sharks.
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Science News (ISSN 0036-8423) is published weekly on Saturday, except the last week in December, for \$54.50 for 1 year or \$98.00 for 2 years (foreign postage is \$18.00 additional per year) by Science Service, 1719 N Street, N.W., Washington, DC 20036. Preferred periodicals postage paid at Washington, D.C., and an additional mailing office.

POSTMASTER Send address changes to **Science News**, P.O. Box 1925, Marion, OH 43306. Two to four weeks' notice is required. Old and new addresses, including zip codes, must be provided. Copyright © 2007 by Science Service. Title registered as trademark U.S. and Canadian Patent Offices. Printed in U.S.A. on recycled paper. ♻️
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Skeletal Discovery

Bone cells affect metabolism

If your blood glucose is out of whack, the problem may be in your bones. New research in mice shows that bone cells exert a surprising influence on how the body regulates sugar, energy, and fat.

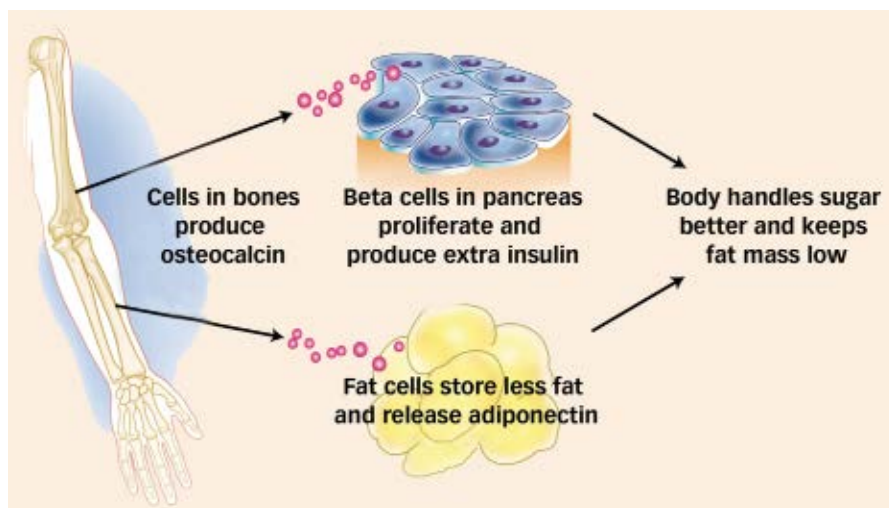
The discovery could lead to new ways to treat type 2 diabetes, a disease involving poor regulation of blood glucose. It also means that skeletons act as endocrine organs, which affect other body tissues by releasing hormones into the bloodstream.

"I'm already changing my teaching slides" about the functions of bones, comments Jennifer Westendorf, an associate professor of orthopedic surgery at the Mayo Clinic in Rochester, Minn. "Now we can add that [the skeleton] affects energy metabolism as well," she says. "It's certainly an exciting breakthrough."

The team announcing the finding, led by Gerard Karsenty of Columbia University, had previously found that fat cells secrete a hormone that influences bone-forming cells called osteoblasts. Because hormone regulation between two cell types is often reciprocal, Karsenty and his team reasoned that osteoblasts might also be emitting hormones that control fat tissue. Osteoblasts make bone throughout a healthy person's lifetime, while cells called osteoclasts tear down bone—processes that constantly remodel the skeleton.

Osteocalcin, a somewhat enigmatic protein produced only by osteoblasts, seemed like a good hormone candidate, Karsenty says. "[It] has been the flagship molecule of the [bone-research] field for 30 years, but nobody knew what it was doing."

Karsenty's team fed a normal diet to mice engineered to lack the gene for osteocalcin. The mice became obese and had low blood concentrations of insulin, a key hormone for controlling blood glucose. The animals also had poor sensitivity to insulin, a hallmark of people with diabetes.



THE ARM BONE'S CONNECTED A bone-cell protein called osteocalcin influences energy metabolism through its effects on pancreatic and fat cells.

Another group of mice, which had been engineered to have extra osteocalcin, stayed thin despite being fed a high-calorie diet. These animals also maintained higher insulin concentrations and better sensitivity to insulin than the mice lacking osteocalcin did, the team reports in the Aug. 10 *Cell*.

Further tests on mice showed that osteocalcin causes the insulin-making cells in the pancreas to proliferate and ramp up insulin production. The bone protein also causes fat cells to store less fat and to secrete a hormone called adiponectin. In people as well as in mice, this substance improves cells' sensitivity to insulin.

Previous research has shown that many people with type 2 diabetes have low blood concentrations of osteocalcin.

"Osteocalcin, if everything goes well, could be a treatment for type 2 diabetes. That's where the excitement is," Karsenty says. Columbia University holds a patent on the idea, and Karsenty says that he's helping form a company to commercialize the treatment.

"This could also have important ramifications for cardiovascular disease because of the effect on metabolic syndrome," a condition related to diabetes, comments Dana T. Graves of Boston University. "The fact that bone cells regulate energy metabolism, and that they do it through osteocalcin, is a major finding," he says. —P. BARRY

Ferrets Gone Wild

Reintroduced animals coming back in Wyoming

The first wild population of endangered black-footed ferrets that started from captive-bred animals, once feared to have

died out, has survived and is growing, researchers say.

The latest survey, from 2006, reports nearly 200 ferrets in Wyoming's Shirley Basin, says Martin Grenier of the University of Wyoming in Laramie. They descend from animals released there between 1991 and 1994. The new census fits in with an exponential population growth that Grenier and his colleagues have seen in surveys since 2000, they say in the Aug. 10 *Science*.

The ferrets' future depends on the well-being of their main food item, the prairie dog. The small ferret population also remains vulnerable to disease. Even so, Grenier and his colleagues say that the resurgence of the Shirley Basin ferrets largely relieves fears that the population's founders were too inbred to reproduce well in the wild.

"The black-footed ferret reintroduction to Shirley Basin is quite a famous case study," says Doug Armstrong of Massey University in Palmerston North, New Zealand, a biologist who studies reintroductions.

North America's only native ferret, the black-footed species has thrived or failed in accord with the fortunes of three prairie dog species on the western plains. Prairie dogs make up 90 percent of the ferrets' diet.

Prairie dog populations declined as people tried to eradicate them and diseases such as sylvatic plague swept the West. The ferrets grew rare too. In the early 1970s, a captive-breeding attempt for ferrets failed when a vaccine against canine distemper that had worked safely in domestic ferrets gave wild ones the disease.

Biologists thought that wild ferrets then went extinct, but in 1981 a rancher's dog rediscovered the animals near Meeteetse, Wyo. State wildlife managers trapped as many as they could—18 animals—for another try at breeding the black-footed ferret in captivity.

"We were thinking it was similar to the

domestic ferret, but it wasn't similar at all," remembers reproductive physiologist JoGayle Howard of the Smithsonian Institution's National Zoological Park in Washington, D.C. She and others eventually persuaded seven ferrets to breed, and from that initial group more than 4,800 kits have been raised.

The first reintroduced animals, 228 in all, went to the Shirley Basin, where prairie dogs inhabit some 150 acres. Sylvatic plague hit the prairie dogs—and biologists discovered that they had been wrong in believing that ferrets were immune.

Since then, captive-bred ferrets have been released in 12 other places. At least two populations seem to be thriving, although they haven't been surveyed, says Grenier.

Surveying the animals and what affects them after the release is "a key part of any reintroduction," says Philip J. Seddon of the University of Otago in Dunedin, New Zealand. He decries the "bad old days of species reintroductions of 'Let's just chuck them out there and come back later to see if any survived.'"

Reintroduced animals need a place where they're protected from whatever menaced them in the first place, notes Seddon. "An example is the Arabian oryx in



SECOND LIFE After almost going extinct in the wild in the 1970s, black-footed ferrets have bred in captivity. Now, a population is increasing in the wild.

Oman, held up as a success with a healthy, self-sustaining wild population before collapsing following resumption of poaching."

Howard says, "It comes down to habitat." —S. MILIUS

Bad for Baby

New risks found for plastic constituent

Two animal studies demonstrate that early exposure to a chemical known to leach from baby bottles, the linings of food cans, and other plastic items can trigger illness and even changes in genetic expression. A building block of polycarbonate plastics, bisphenol A (BPA) ends up in food, people, and the environment.

In one of the new studies, the pollutant permanently reprogrammed a gene in pups of mice fed BPA-laced chow.

The mice carried the *Agouti* gene, which is particularly vulnerable to what are called epigenetic changes. In such effects, hormones and other agents typically remove chemical units known as methyl groups from genes, or add them, interfering with the genes' function. Epigenetically affected *Agouti* mice, normally lean and brown-haired, become fat and blond (*SN*: 6/24/06, p. 392).

Randy L. Jirtle and his colleagues at Duke University in Durham, N.C., fed female mice chow that delivered 50 milligrams of BPA daily per kilogram of body weight throughout the animals' pregnancies and lactation periods. Blond fur and obesity in pups demonstrated *Agouti* reprogramming, say the researchers.

However, supplementing the mothers' diet with methyl-donating agents such as folate blocked BPA's epigenetic impacts, Jirtle's team reports in the Aug. 7 *Proceedings of the National Academy of Sciences*.

In a second study, Retha R. Newbold's team at the National Institute of Environmental Health Sciences (NIEHS) in Research Triangle Park, N.C., exposed newborn female mice to BPA for 5 days. Injected under the skin, doses ranged from 10 to 1,000 micrograms per kg of body weight.

Eighteen months later, the researchers examined the middle-aged animals' reproductive tracts and found more fertility-jeopardizing impairments than in a group of untreated mice. Problems included cysts inside and outside the ovaries, development of glands in inappropriate places in the uterine lining, and polyps or other excessive-tissue growths in or on the uterine lining. Newbold's group reports its findings online and in an upcoming *Reproductive Toxicology*.

The brief BPA doses delivered to the reproductive organs of affected mice "are below the levels measured in the serum of human

adults today," Newbold told *Science News*.

Reproductive Toxicology is also publishing five reviews of BPA studies and a consensus statement signed by 38 researchers who last fall took part in an NIEHS-sponsored expert-review conference on low-dose effects of the pollutant. Generally, the new reports and the consensus statement conclude that animals can be harmed by BPA at body burdens below those found in most adult residents of industrial nations.

Steven G. Hentges of the American Chemistry Council in Arlington, Va., finds both the Jirtle and Newbold teams' studies of academic interest but argues that neither contributes much to the debate on human health. In one instance, says Hentges, the doses in mice were too large, and the other study was based on injected doses, which he terms irrelevant for assessing risks to people.

Frederick S. vom Saal of the University of Missouri-Columbia disagrees. He and other participants at NIEHS' BPA-review conference concluded that injecting BPA is appropriate for modeling exposures, especially in young animals. Moreover, the Duke group's study provides the evidence confirming researchers' suspicions that BPA can exert epigenetic changes, says vom Saal. —J. RALOFF

Nerve Link

Alzheimer's suspect shows up in glaucoma

A protein fragment that litters the brains of people with Alzheimer's disease may also bear responsibility for some of the vision loss in glaucoma, a new study in rats shows.

Glaucoma patients typically have abnormal fluid pressure within the eye, but it remains unknown how this stress kills the nerve cells at the back of the retina. While there is no cure for glaucoma, easing eye pressure with drugs or surgery helps prevent vision loss in many patients.

Some glaucoma patients, however, experience vision loss even with normal eye pressure, indicating that other factors are sometimes involved.

The new research suggests that one hidden assailant is amyloid-beta, the same protein fragment that accumulates in the brains of Alzheimer's patients. An earlier rodent study of glaucoma had found the substance in the animals' eyes, but other evidence of amyloid-beta in glaucoma is scarce.

In the new study, ophthalmologist M. Francesca Cordeiro of University College London and her colleagues induced glaucoma in 60 rats by injecting saline into the animals' eyes. Within weeks, amyloid-beta deposits showed up in dying retinal-nerve cells.

The researchers then gave another round of eye injections to some of the rats. In one eye, the animals received a synthetic antibody that absorbs amyloid-beta. The other eye got a placebo.

After 3 weeks, the medicated eyes showed only one-fourth as much retinal-cell death as did the untreated eyes, the researchers report in an upcoming *Proceedings of the National Academy of Sciences*. The effect remained 13 weeks later.

Next, the scientists repeated the experiment on other rats with glaucoma, this time using a cocktail that included the antibody and two other drugs with anti-amyloid-beta effects: a dye called Congo red and an enzyme deactivator called beta-secretase inhibitor. The triple combination worked even better than the antibody alone, reducing cell death by 84 percent.

"This offers a novel hypothesis and very intriguing results with the potential for therapeutic impact on a devastating, blinding disease," says psychiatrist Lee E. Goldstein of Harvard Medical School and the Brigham and Women's Hospital in Boston. It remains unclear, though, whether amyloid-beta is similarly involved in human glaucoma and, if so, whether it's a perpetrator of the disease or a bystander. "The jury is still out," says Goldstein.

Researchers are currently testing an amyloid-beta antibody as a drug in a large trial of Alzheimer's patients, but Congo red and beta-secretase inhibitor haven't entered that stage of Alzheimer's testing, Cordeiro says. She says she's hopeful that scientists will assess the triple combination in glaucoma patients within 2 or 3 years.

"One of the problems I have as a glaucoma doctor is that there are no other real treatments out there, other than reducing pressure in the eye," she says. —N. SEPPA

Drug Overflow

Pharmaceutical factories foul waters in India

Pharmaceuticals ranging from painkillers to synthetic estrogens can harm aquatic life when they enter waterways through human excreta, hospital and household waste, and agricultural runoff. Now, researchers have shown that there's another way for such drugs to get into the environment: A treat-

ment plant in India that processes wastewater from pharmaceutical manufacturers discharges highly drug-contaminated water into a stream that feeds a major river.

The treated water contained astronomical amounts of antibiotics, along with high concentrations of analgesics, hypertension drugs, and antidepressants.

Production facilities "have not been considered an important source of drugs in [the] environment," says lead author Joakim Larsson of Göteborg University in Sweden. "This is not the case in India. We found levels of drugs many orders of magnitude higher than anywhere [recorded] on Earth before."

Larsson and his colleagues collected water samples from the effluent of a treatment plant that cleans the wastewater of 90 bulk-drug manufacturers in Hyderabad in southern India. The region produces most of India's pharmaceuticals, 60 percent of which are exported. The treated effluent pours into a stream that eventually joins the Godavari, India's second-largest river.

Of the 59 compounds for which researchers screened, 21 were present in concentrations greater than those typical of drugs in effluent from U.S. sewage-treatment plants, about 1 part per billion (ppb). Eleven of the drugs, including six antibiotics, had concentrations higher than 100 ppb. One of them, the common broad-spectrum antibiotic ciprofloxacin, registered at about 30,000 ppb. An antidepressant that belongs to a class of drugs known to disrupt hormone effects in fish (*SN*: 6/17/00, p. 388) was at a concentration of 800 ppb.

The results appear online and in an upcoming *Journal of Hazardous Materials*.

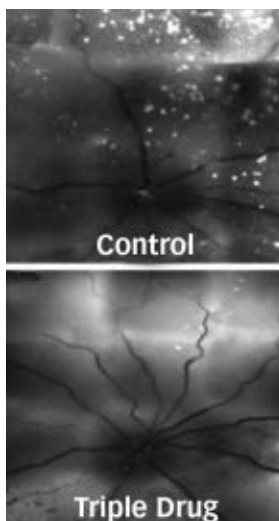
Beyond studies of gender effects in fish, little research exists on the possible health effects on people and other animals of pharmaceuticals in the water supply. However, Larsson points out that the amount of antibiotics that his team found was well above that known to affect a variety of organisms, including plants, bacteria, and blue-green algae (*SN*: 6/29/02, p. 406). "There is no doubt" that concentrations found in the study are toxic, he says.

Following common practice, the treatment plant in India mixes raw human sewage with contaminated waste to enlist the decomposing capacity of bacteria in the water cleanup. The enormous quantities of antibiotics in the wastewater might not only reduce the effectiveness of that process but

also encourage the development of antibiotic-resistant bacteria, Larsson says.

"We do find pharmaceuticals routinely in wastewater effluents," says Dana Kolpin, a hydrologist with the U.S. Geological Survey in Iowa City, Iowa. The concentrations recorded in the study are "certainly significant," he says. Sampling incoming waste and the sludge remaining after treatment, he says, would clarify what quantities of drugs are getting into the environment.

Daniel Schlenk, an ecotoxicologist at the University of California, Riverside, notes that many of the drugs measured in the new study are water soluble and are more likely to be diluted and washed away than to accumulate in aquatic organisms. Even so, the extremely high concentrations recorded "could still be a problem," he says. —C. BARRY

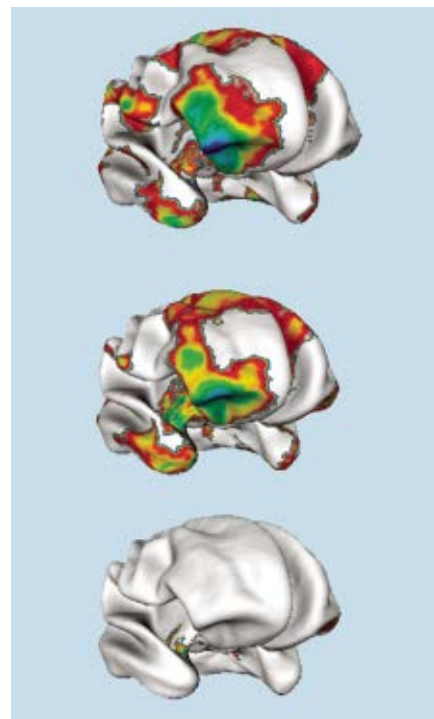


DEAD EYE White specks are dying nerve cells in retinas of rats with glaucoma. The retina at bottom was treated with three drugs that inhibit amyloid-beta production. Black lines are blood vessels.

Bad News, Good News

ADHD-risk gene has silver lining

A gene variant that increases the risk for attention-deficit hyperactivity disorder also appears to help children grow out of the worst of their behavioral problems as certain brain structures normalize, new research suggests.



GETTING BETTER In 8-year-old children with ADHD who carry a certain gene variant, some brain regions are unusually thin (colored areas, top image). The differences diminish by age 12 (middle) and almost disappear by age 16 (bottom).

"It looks like a double-edged sword," Philip Shaw says of the gene variant. Shaw led the work at the National Institute of Mental Health in Bethesda, Md.

Previous research found that children with a particular version of the *DRD4* gene had an additional 15 to 45 percent risk of being diagnosed with ADHD. It's the strongest known heritable risk factor for the disorder, which affects an estimated 3 to 6 percent of school-age children in the United States.

Last year, Shaw and colleagues reported that certain brain regions in children carrying this gene variant were unusually thin. That finding buttressed theories suggesting that those regions, on the right side of the brain's outer layer, or cortex, serve as attention centers.

Shaw's team now finds that in those same children the affected brain regions normalize in thickness during adolescence. At age 8, children carrying the gene variant had a much thinner-than-normal cortex in the key areas, but by age 16 those differences had all but disappeared.

At the same time, behavioral symptoms such as poor concentration and weak impulse control improved more in ADHD children with the gene variant than in ADHD children who carried other versions of the gene. After 6 years in the study, 79 percent of children with the gene variant had shed the diagnosis, compared with only 49 percent of the other children.

Shaw and his colleagues looked at brain scans and DNA from 105 children with ADHD and from 103 children without the disorder; they report in the August *Archives of General Psychiatry*. Overall, 45 percent of the children with ADHD had the gene variant in question, and 34 percent of non-ADHD children had it.

The new research builds on prior evidence that youngsters with ADHD, who lack concentration, self-control, and organizational skills, possess smaller brain volumes than psychiatrically healthy children do (*SN*: 10/12/02, p. 227). The findings also bolster the case that the brain's dopamine system is impaired in ADHD, says Shaw. Dopamine is a key nerve-signaling molecule. The *DRD4* gene encodes a dopamine receptor, a lock-like molecule that triggers nerve activity when dopamine fits into it like a key. Methylphenidate (Ritalin) and other drugs prescribed for ADHD change how the brain responds to dopamine.

In addition, the new research supports the idea that there are at least two subtypes

of ADHD, says James Swanson of the University of California, Irvine. His research shows that children carrying the *DRD4* variant don't have the cognitive impairment shown by some children with ADHD.

"I think there is a personality characteristic that leads to the diagnosis of ADHD related to the *DRD4* gene," he says. "Then you have another group that's ADHD because they have some sort of minimal brain damage" that's probably not in the part of the brain affected by the gene variant. —B. VASTAG

Newton's Dusty Mirror

Old experiment inspires ultrafast imaging

Occasionally, science museums can stimulate new science. Inspired by an exhibit on an optical experiment performed by Isaac Newton, physicists have taken the first X-ray snapshot of a microscopic explosion.

Physicists Henry Chapman and Saša Bajt took their daughter to the Chabot Space and Science Center in Oakland, Calif., in 2005. There, they saw a replica of an experiment in which Newton had sent a beam of light through a hole in a screen. The beam reflected off a mirror and back onto the screen—where Newton was surprised to see concentric rings of light.

Scientists later determined that the rings were due to microscopic specks of dust. Light bounced off each dust grain twice, on its way to the reflective surface and on the way back. Interference between those two sources of scattered light, as crests and troughs of their waves either reinforced or canceled each other, created the rings.

Chapman and Bajt, both of Lawrence Livermore (Calif.) National Laboratory,

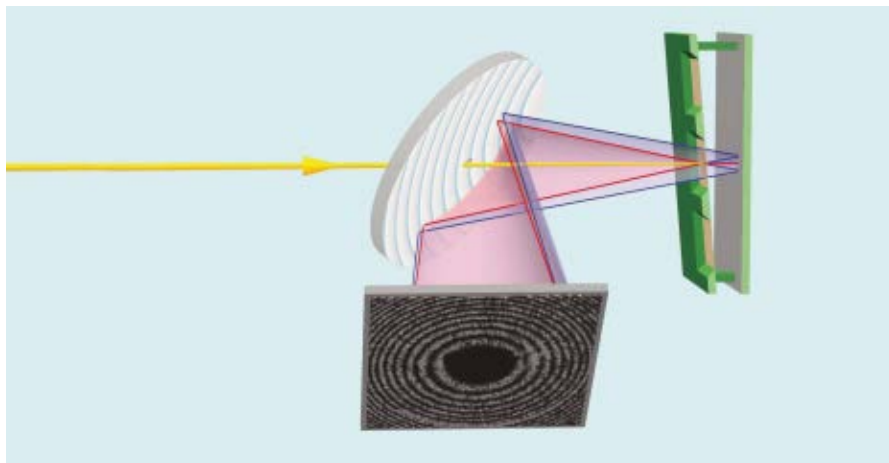
realized that they could set up a similar experiment at FLASH, a laser facility in Hamburg, Germany. FLASH is the first free-electron laser to operate in the extreme ultraviolet, or soft-X-ray, part of the spectrum. Free-electron lasers use bursts of electrons to create pulses of laser light lasting only femtoseconds, or millionths of a billionth of a second. These devices could in a few years create high-energy, or hard, X rays that have wavelengths small enough to resolve single atoms.

Such bursts of energy would explode most samples. But scientists hope that the bursts will be short enough—lasting as little as a single femtosecond—that X rays can pass through the sample and carry off information before the sample's atoms have moved appreciably (*SN*: 4/21/07, p. 253).

To better understand the dynamics of such an explosion, Bajt, Chapman, and their collaborators sent soft X rays from the FLASH laser through a hole in the non-reflecting side of a mirror and onto plastic balls, just 140 nanometers wide, fixed to a thin membrane. The beam then bounced off a second mirror and hit the balls again, hundreds of femtoseconds later. X rays scattered in those two encounters reflected from the first mirror and onto a detector, where they formed concentric circles.

From the size of these interference fringes, the scientists reconstructed the shapes of the balls as they shattered. By adjusting the position of the second mirror, the scientists took snapshots at different time intervals. "It was the first time we have been able to measure the explosion," Chapman says. The team reports its results in the Aug. 9 *Nature*.

Andrea Cavalleri of the University of Oxford in England says that the experiment "gives hope" that hard-X-ray lasers will be able to observe femtosecond-scale dynamical processes, such as chemical reactions, down to the resolution of single atoms. —D. CASTELVECCHI



NEWTON REVISITED An X-ray beam (yellow) passes through one mirror, blows up a microscopic particle suspended on a membrane (in green frame), bounces off a second mirror (right), and hits the exploding particle again. Interference fringes (full circles) capture the explosion.

Can We Get a Clear Picture of Jesus from the Gospels?

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be, how they are related to one another, and how they communicate through their literary structure, plot, character development, themes, and symbolism. After all, it is as literature that the Gospels influenced history. And it is through literature that present-day readers can continue to encounter Jesus.

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TAKING A JAB AT CANCER

Combined with drugs, vaccines against tumors may finally be working

BY PATRICK BARRY

Imagine a patient getting a vaccine injection in the doctor's office—but not to ward off a virus or a bacterium that causes smallpox, measles, or any other infectious disease. This vaccine is for cancer, specifically for a tumor already growing within the patient's body. The treatment, perhaps in combination with others, is intended to train the patient's immune system to recognize and kill malignant cells.

It's a strategy that scientists have been working on for more than 15 years, but rallying the immune system to fight cancer has proved more difficult than most people expected. Designing a cancer vaccine requires a deep understanding of the immune system's intricacies—knowledge that has come about only in the past few years. In addition, cancer cells can flip chemical switches to subvert attacks by the immune system, adding a layer of difficulty to vaccine design.

To date, no cancer vaccine has been approved by the U.S. Food and Drug Administration. The vaccine against cervical cancer that's been in the headlines is a conventional preventive vaccine that targets the virus that causes cervical cancer.

The only therapeutic cancer vaccine that's come close to approval is a prostate cancer treatment called sipuleucel-T. In March, an FDA advisory panel gave sipuleucel-T the thumbs-up, but the agency decided to delay approval pending the completion of a large trial in men with prostate cancer.

"The reality is that [the field] has been and continues to be waiting for a clear clinical success," says Drew Pardoll, professor of oncology at Johns Hopkins University in Baltimore.

Recent research has not only revealed the switches that tumor cells flip to defuse an attack from the immune system, but has also yielded possible drugs to counteract this ploy. Paired with vaccines, several of these new drugs appear to be able to unleash the potential of the vaccines to spur the immune system to attack cancer cells.

Many researchers say that these "combinatorial" therapies could be the way forward for cancer-vaccine research. "We can beat this disease with the immune system with the right kinds of combinatorial approaches," Pardoll says.

SUBTERFUGE AND BETRAYAL In their housecleaning role, roving sentries of the immune system identify and destroy badly damaged cells in the body. But cancer cells, which by definition are damaged cells that grow and proliferate unchecked, are surprisingly crafty adversaries.

The immune system has control mechanisms to prevent immune cells from attacking the body's healthy cells. As part of this control system, killer T cells, the immune system's attack dogs, require multiple signals before they'll swing into action.

First, they need immune cells called dendritic cells to chew up a sample of the target and present a piece to the killer T cell as an example of what to look for. Dendritic cells play a key role in activating an immune response—whether against a foreign microbe or a damaged body cell—so many of the most promising new cancer vaccines use dendritic cells to train the immune system to recognize tumor cells. Sipuleucel-T is one such product.

But to activate killer T cells, or killer Ts, so-called helper T cells must release chemical cues. Regulatory T cells (T-regs), yet another kind of cell, function as the brakes of the immune system by producing compounds that keep killer Ts in check.

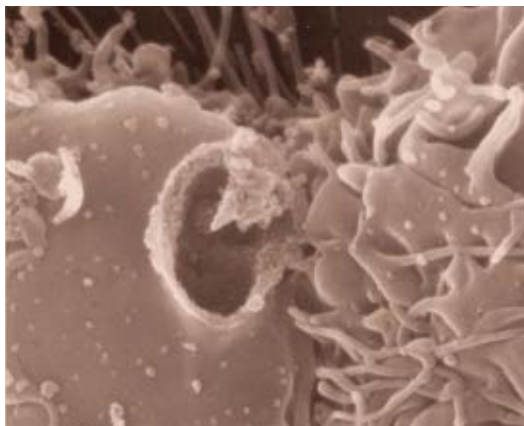
Tumors manipulate these elaborate control mechanisms to fool the immune system into treating cancer cells like friends instead of foes, a phenomenon called tolerance. "This is the central mission of the field—to selectively break tolerance to these tumors," Pardoll says.

For example, cancer cells emit a protein called vascular endothelial growth factor (VEGF), which triggers the creation of new blood vessels to feed the fast-growing tumor. Conveniently for the tumor, VEGF also stifles the maturation of dendritic cells. Keeping dendritic cells stuck in an immature state prevents them from performing their critical role of training and activating killer Ts. What's more, these immature dendritic cells actually stimulate T-regs, which suppress the immune response even further. Dendritic-cell development is also hindered by other tumor compounds, including the immune-signaling molecules interleukin 6 and 10, a substance called transforming growth factor-beta, and the inflammation-related enzyme cyclooxygenase-2.

Cancer cells can also release chemical signals that recruit T-regs and draw them into the tumor. "We know that these T-regs are sitting in the cancer and actually deactivating the [killer] T cells," says Elizabeth M. Jaffee of the Sidney Kimmel Cancer Center at Johns Hopkins.

Ironically, it's often the immune system itself that pushes cancer cells to such nefarious lengths. Scientists have confirmed in recent years that a person's immune system has an innate ability to detect and kill some precancerous cells.

However, sooner or later, one of these precancerous cells will mutate such that it begins producing some of the signaling molecules that protect it against attack. In the same way that the overuse of antibiotics drives the evolution of drug-resistant "superbugs," the immune system applies an evolutionary pressure on



THE CURE WITHIN — This multilobed killer T cell, part of the immune system, is destroying a cancer cell. But tumors can undermine such attacks.

precancerous cells that pushes them to develop defenses against it. The cell in which that pivotal defensive mutation occurs is then free to proliferate wildly and to develop into full-blown cancer.

"We've come to look at the development of cancer in a person as an evolutionary struggle between rapidly mutating cells and the immune system," says Louis M. Weiner of the Fox Chase Cancer Center in Philadelphia.

DECLOAKING TUMOR CELLS The latest strategy in cancer vaccines combines them with drugs that subvert these sophisticated defenses of tumors. By disabling the stop signals that cancer cells send to a person's immune system, these combination therapies should enable vaccines to do their jobs and spur immune cells into action against tumors. Experiments in mice and early trials in cancer patients are beginning to show that scientists might finally be on the right track.

"There are [experimental] vaccines now that are going into patients that are so much more potent at breaking tolerance than has ever been seen in the vaccines from the previous era," Pardoll says.

One promising strategy involves combining vaccines with drugs that block the action of a protein called cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4). This substance sits on the surface of T cells, and when activated, suppresses killer Ts' tumor-fighting activity. Blocking CTLA-4 can release this brake on the immune system.

A small trial in patients in the Netherlands combined a CTLA-4 blocker called ipilimumab with an experimental cancer vaccine called GVAX. At the 2007 conference of the American Society of Clinical Oncology in Chicago, Winald Gerritsen of the Free University Medical Center in Amsterdam and his colleagues announced that the combination treatment reduced blood concentrations of prostate-specific antigen, a protein produced in excess by abnormal prostate cells, in 5 of 6 prostate cancer patients.

Tests of the patients' immune system activity showed that their killer Ts and dendritic cells had become activated, indicating that the drug had released the checks on these cells so that the vaccine could rally them to action. With so few people in the trial, the results are only provisional, but "you have to sit up and take notice," Pardoll says.

"If you saw results like this in larger trials, it would be almost unprecedented," says Jeffrey Schlom, chief of the Laboratory of Tumor Immunology and Biology at the National Cancer Institute in Bethesda, Md.

Studies of similar combination therapies in mice have produced even more dramatic results. A team led by James P. Allison of the Memorial Sloan-Kettering Cancer Center in New York City treated mice with skin cancer using a similar therapy of GVAX with a CTLA-4 blocker. The treatment eliminated tumors in more than 90 percent of the mice, the team reported in the July 2006 *Journal of Clinical Investigation*. The balance between the numbers of killer T cells and T-regs within the tumor clearly shifted in favor of killer Ts, showing that the combo therapy weakened the cancer's defenses and released the brakes on the immune system.

Unfortunately, releasing these brakes can also have adverse effects. In the Netherlands study, for example, most of the patients developed significant loss of kidney and thyroid function as well as flu-

like symptoms, all presumably due to the patients' immune systems attacking healthy cells in their bodies.

Another strategy involves pairing a vaccine with a compound that inhibits T-regs. Suppressing T-regs removes the brake on killer Ts, allowing them to mount an attack against the tumor. One particularly effective T-reg suppressor is the chemotherapy drug cyclophosphamide. François Martin and his colleagues at the French National Institute of Hygiene in Dijon showed in 2004 that giving rats with colon cancer cyclophosphamide along with a cancer vaccine enabled their immune systems to destroy the tumors, while the vaccine alone could not.

"Finding ways to reduce T-regs is one of the most promising things going on in the field," says Jarrod Holmes of the Cancer Vaccine Development Lab in Bethesda, Md.

VEGF also provides a ripe target for drugs. Drugs that block

VEGF allow dendritic cells to mature, thus improving the effectiveness of cancer vaccines, as Leisha A. Emens of the Johns Hopkins University School of Medicine and her colleagues report in the July 1 *Clinical Cancer Research*. The researchers found that a cancer vaccine for breast cancer shrank tumors in mice more quickly when given with a VEGF inhibitor called DC101. Suppressing T-regs by adding cyclophosphamide to the mix made the cancer-fighting effect of the combination even stronger.

ROUND PEG, SQUARE HOLE

Although researchers in the field are optimistic, these combination vaccines are moving through the drug-development pipeline toward larger trials very slowly.

Because drugs are normally tested and approved one at a time, the industry is organized around single-drug development. This structural bias against multiagent

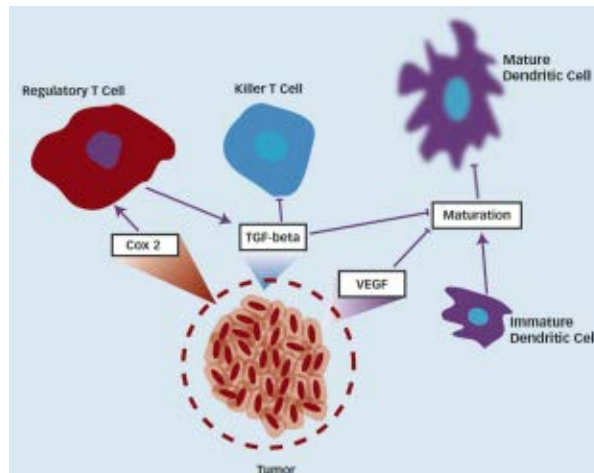
therapies has hampered the development of these new vaccines, researchers say. Vaccines that are farthest along in the approval process, such as the prostate cancer treatment sipuleucel-T, generally aren't combination therapies.

"I'm not saying that it's anyone's fault," Jaffee says, "but unfortunately, the way our process for drug development is, it's very slow if you want to get approval for more than one agent."

Normally, each component of the treatment must make it through human trials on its own. And to pass the trials, a drug must be more than just safe; it must also be effective. Often, contend Jaffee and others, the components of a combination vaccine are effective at killing tumors only when used together, making it difficult to get a component approved on its own.

Scientists are afraid of trying combined vaccine-drug therapies until each component is FDA approved, Schlom says. A scientist who combines an unapproved drug with an experimental vaccine puts both compounds at risk of never reaching the market and the clinic. If early trials of the combo show toxic effects in people, it may be impossible to justify further trials of the compounds, even though the cause of the toxic effects—be it the drug, the vaccine, or the synergy of the two—may be unknown.

With these policy challenges, as well as formidable research obstacles, to overcome, the field certainly has a long way to go. But recent progress hints at the unique payoff that's possible with cancer vaccines. "The future is very, very bright," Pardoll says. ■



WEB OF DECEIT — Tumor cells send out chemical signals such as vascular endothelial growth factor (VEGF), transforming growth factor beta (TGF-beta), and cyclooxygenase-2 (COX2) that reduce the immune system's attack on the cancer. Activation steps (arrows) and inhibition (lines with bars) boost regulatory T cells, curb killer T cells, and stifle the maturation of dendritic cells. Immature dendritic cells and stimulated regulatory Ts further subdue the antitumor response of the killer Ts.

HAMMERED SAWS

Shark relatives with threatening snouts win global protection

BY JANET RALOFF

The sawfish features one of Mother Nature's oddest designs. Its flat snout resembles a chain saw with dozens of toothlike minidaggers. When the predator encounters a school of fish, it slashes its saw from side to side. As the injured quarry flutters in the water, the sawfish hoists its snout skyward and vacuums in dinner.

Sawfish can grow to 6 meters or more in length. Even newborn pups have a commanding presence. Born live, 6 to 12 at a time, each pup enters the world at almost a meter long, toothy saw in place.

These predators tend to inhabit coastal bays and lagoons. However, they can be found inland as well, cruising brackish rivers and even the occasional freshwater lake.

Sawfish became a powerful symbol in many cultures. Aztecs revered this cousin of the shark as an "Earth monster." Some Asian shamans still brandish its toothy snout in exorcisms and other ceremonies to repel demons and disease. Chinese chefs prize sawfish fins for a luxury soup.

For millennia, warm coastal waters around the world teemed with these mighty predators. Over the past 2 centuries, however, fishing fleets with ever-growing nets have snagged countless numbers of the behemoths—mostly unintentionally. Considering the fish a nuisance, fishers gave little thought to extracting the sawfish and returning them to the sea alive. Eventually, a trophy market developed for the animals' awesome snouts.

More recently, sawfish have been disappearing because of a strong and growing market in Asia for their fins. Owing to their scarcity, a pair of those fins can cost up to \$3,000 in some Asian specialty markets today.

Even among biologists, these fish were "never on the radar screen," says John Carlson of the National Marine Fisheries Service in Panama City, Fla. Not surprisingly, he says, their virtual disappearance in the 1970s went unnoticed.

No one knows the full effects of waning sawfish numbers on coastal ecosystems, largely because little research was performed on the fish while they were still dominant predators.

Beginning next month, however, all seven of the world's known species of sawfish will gain protection under a United Nations-administered treaty. The Convention on the International Trade in Endangered Species, or CITES, will ban international sales of sawfish, dead or alive, whole or in pieces. The goal is to motivate fishers to release every sawfish that they capture.

Biologists and marine conservationists hope the move is coming soon enough for the populations to make comebacks. Although most sharks and shark relatives are overexploited, "I don't think you'd get any argument that sawfish are the most endangered," says Sonja Fordham of the Ocean Conservancy, based in Washington, D.C.



MONSTROUS — This January 1933 picture shows British adventurer F.A. Mitchell-Hedges and a member of his traveling party with a 10-meter-long sawfish caught in the Caribbean. Today, finding sawfish more than about 3 meters long is unusual.

BIO INCOGNITO Sawfish are rays, and as such, they're essentially flattened sharks with wings. Like other shark relatives, rays mature slowly and reproduce at immensely lower rates than most fish do. This makes the animals especially slow to recover from overfishing.

The result is that sawfish have been snagged by fishing fleets faster than they can reproduce.

Records from just one region of Florida, near Cape Canaveral, illustrate the magnitude of fishing's impacts. A 19th-century fish survey there identified sawfish as "among the most abundant species in the Indian River system." One local mullet fisherman reported catching 300 sawfish in a single season. But when biologists surveyed the Indian River region in 1981, not a single sawfish specimen turned up.

Two sawfish species, smalltooths and largetooths, were once widespread along the Western Atlantic from Mexico to New York. Today, remnant North American populations of the smalltooth species (*Pristis pectinata*) persist in south Florida and the Bahamas. Total population numbers have fallen by an estimated 90 percent from prefishing abundances. Largetooth sawfish (*Pristis perotteti*) haven't been sighted in North America since the 1970s.

In 1997, recognizing that sawfish populations had crashed globally, U.S. biologists proposed protecting these fish under CITES. A committee convened under the treaty rejected the proposal, however, for lack of proof that international trade was damaging sawfish populations.

The following year, the Ocean Conservancy petitioned to have the smalltooth species added to the U.S. Endangered Species List. That's when U.S. scientists learned that few data of any kind existed for sawfish anywhere. "This fish had never been formally studied

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in the United States,” notes Tonya Wiley of the Mote Marine Laboratory in Sarasota, Fla. “We didn’t know such basic things as where they live, what habitat they use, how often they reproduce, how many young they have—even what age sawfish are when they reach sexual maturity.”

Wiley and others began poring over decades’ worth of news accounts and scientific-journal articles that mention the fish. The researchers learned, for example, that shrimp trawlers in the Gulf of Mexico reported large accidental catches into the 1960s. Then, during just a 5-year period, reported sawfish catches fell to zero.

In 2001, Carlson’s research team and the Mote Marine Laboratory initiated collaborative field studies of sawfish. Their findings confirmed the animals’ dire status.

“We don’t have any hard numbers on how many remain,” Wiley says, “but our guesstimate is that there are maybe 3,000 to 6,000” in U.S. waters. In 2003, the smalltooth sawfish won the dubious distinction of being the first animal that can spend its entire life in the ocean to be put on the U.S. Endangered Species List.

Its largetooth cousin is now considered extinct in the United States, but small populations remain along the Atlantic coast of Central and South America.

BEHAVIOR ASSESSMENTS Although gaping holes remain, an understanding of sawfish biology is emerging from ongoing field studies. For instance, it appears that smalltooth sawfish don’t reproduce until they’re 3.5 to 4 m long and 10 to 12 years old, notes Wiley. Mom gives birth in shallow waters in spring and then disappears, while her pups remain at their natal beach for months to years.

In the Everglades, baby sawfish may “spend their entire first year or two on a single shallow mud bank” of less than 1 acre, notes Colin Simpfordorfer of James Cook University in Townsville, Australia. He says that juveniles often remain “in just a couple inches of water,” probably to avoid attacks by bull sharks.

Sawfish, like bull sharks, welcome murky water and tolerate low salinity. They can even live in fresh water for months. Although adult sawfish eat fish, juveniles use their saws like shovels to excavate crabs and other marine life from sediments.

Researchers aren’t sure where the pups migrate after leaving their nurseries. Although sawfish are widely regarded as coastal dwellers, scuba divers have spied some adults at the edge of the continental shelf, in waters about 100 m deep. “We’re also learning that they’re quite mobile,” Simpfordorfer says. Satellite tags show them traveling up to 160 kilometers over a 3-month period.

Migration patterns may challenge any conservation strategy, since few places outside of U.S. waters prohibit smalltooth-sawfish capture. The Bahamas, where coastal development is destroying sawfish habitat, for instance, lie 100 km from the prohibited zone. If sawfish migrate from the birthing lagoons in Florida out beyond U.S. waters, protecting them may require cooperation from other nations.

CULTURAL SIGNIFICANCE For the past 500 years or longer, people in many parts of the world have prized the sawfish for its symbolism, notes Matthew T. McDavitt, a Charlottesville, Va.-based attorney who initially trained as an anthropologist. For the past decade, he’s focused many of his off-hours on sawfish studies.

As an undergraduate at the University of Virginia studying Aztec



SO SHALLOW — Sawfish spend the first year or two of life in coastal water that’s often just a few centimeters deep.

art, McDavitt grew curious about painted images of sea creatures resembling sawfish. Further research revealed that Aztec society regarded the sawfish as emblematic of a mythic monster. This finding proved consistent with what anthropologists found in the 1980s, buried beneath the Aztec Great Temple in the center of what is now Mexico City: dozens of sawfish snouts.

“That got me very excited about looking at sawfish elsewhere,” says McDavitt. His next investigation turned up “a pan-Asian belief that the toothy snout of sawfish is the most efficacious tool for repelling demons, disease spirits, and ghosts,” he says.

The online auction site eBay has become a major marketplace for those snouts, known as rostra. Beginning in February 2003, McDavitt charted rostra in eBay auctions daily for an entire year. More than 200 of the items were traded, almost 40 percent going from sellers in the United States to foreign buyers. Some rostras sold for as little as \$40, but a 5-foot-long specimen commanded nearly \$1,600.

One of the odder markets for sawfish parts is trade in rostral teeth, which cockfight operators fashion into artificial spurs for roosters. In his research, McDavitt learned that each rostral tooth is split to yield sharp, thin spurs. Cockfighters prefer the sawfish

material because compared with horn, shell, sea lion teeth, and stingray spines—all of which are sometimes used—rostral teeth are more durable, flexible, and damaging to an opponent.

Patricia Charvet-Almeida of the University of Paraiba in Brazil reported 3 years ago that a pair of spurs can cost almost \$50. With a single snout holding anywhere from 28 to 68 teeth, each of which makes about four spurs, Charvet-Almeida notes that the retail value of a rostrum could top \$6,000.

McDavitt’s probes showed, however, that the biggest sawfish market by far is for fins that go into soup. Although the sawfish is not a true shark, its fins are used in the same way as sharks’ are for shark-fin soup. After many hours of simmering, long cartilage needles, known as ceratrotichia, turn into the gel-like noodles that characterize shark-fin soup, a long-revered food in some cultures (*SN: 10/12/02, p. 232*). In fact, people value sawfish fins so much as a dense source of ceratrotichia that the fish’s fins are among the priciest, at up to \$550 per pound.

It was detailed and compelling data of this sort, much of it from McDavitt, that

convinced international negotiators on June 11 to extend CITES protection to sawfish, says Carlson.

NOW WHAT? The United States accepts CITES listings as grounds for ending even domestic trade in a species. “Each country implements CITES with its own legislation,” however, says Nancy Daves of the National Oceanic and Atmospheric Admin-



ROUTINE CHECKUP — When, on rare occasions, researchers catch a sawfish, they measure it and extract a tiny bit of flesh—for DNA analysis—before returning the fish to the water.

istration's fisheries service. Enforcement and penalties vary, and some countries still allow trade within their borders.

The real impetus behind the CITES listing and ongoing research is not only to limit trade in sawfish, but also to foster the species' recovery. The United States has been developing a recovery plan for its domestic smalltooth sawfish. The plan will focus on current knowledge about the animal in an effort to identify habitat that needs to be saved, educate fishers to recognize and release any sawfish that they might pull in, and coordinate further research.

Recently, several researchers have been studying sawfish genetics. For instance, Demian Chapman, head of the Pew Institute for Ocean Science's shark program at the University of Miami, is cataloging portions of the smalltooth-sawfish genome where snippets of DNA repeat many times. These genetic bits, known as DNA microsatellites, are highly susceptible to mutation over short periods of time, says Chapman, so biologists can compare them to determine how closely related individuals are.

Without harming a captured fish, biologists can take a tiny plug of tissue and send it to an analyst such as Chapman. By comparing microsatellite profiles in two fish at up to 15 spots along the specimens' DNA, he hopes to tell whether or not the fish come from the same population.

Even if research shows that small communities of sawfish develop with little interbreeding, the DNA data should fill some basic

research gaps. The information could explain, for instance, how many discrete breeding populations remain in any area.

"Our goal is to develop enough of these markers that we can recognize kin," says Chapman. If done over several years, such testing might also identify distinct broods, which could reveal how frequently females give birth.

Although the microsatellites that Chapman is studying come only from U.S. smalltooth sawfish, "there's every chance that some of these markers will work for other sawfish [species]," he says. That would speed efforts to understand what's happening among those declining populations as well.

In Fortaleza, Brazil, Vicente Faria of the National University of Ceará is studying the genetics of hundreds of sawfish specimens from around the world to identify species. Many sawfish that look similar may represent subspecies or entirely different species. Knowing how many distinct genetic groups exist will prove important to their management, since each group would need to be conserved individually.

Faria is also investigating the degree of genetic variability that exists within populations, which may indicate how well a particular population might adapt to a changing environment.

Unfortunately, the bounty paid for sawfish offers a strong economic incentive for poachers to undermine conservation efforts. As one Kenyan biologist explained at the CITES meeting in June, the high value of a single large rostrum means that some indigenous fishers in Africa "can retire after catching one sawfish." ■



TOOTHY TROPHY — A new international-conservation listing will soon trigger prohibitions on U.S.-domestic and country-to-country trade in sawfish and their parts, such as this nearly meter-long *Pristis perotteti* snout. The former museum piece sold on eBay in mid-June.

J. O'DONNELL

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PLANETARY SCIENCE

Deep Impact and Stardust: Still on assignment

Two old NASA missions have new lives. The agency's Deep Impact mission, which 2 years ago fired a projectile into Comet Tempel 1 and imaged the debris from the explosion, will now journey to Comet Boethin.

Deep Impact doesn't have another bullet in its arsenal but will fly peacefully to Boethin, getting to within 700 kilometers of the object on Dec. 5, 2008, so it can obtain close-up images. This year, en route to the comet, the spacecraft will study several nearby, bright stars known to have massive, orbiting planets. Deep Impact will search for periodic variations in starlight as the planets pass in front of and behind their parent stars. The variations may reveal not only the size and composition of the Jupiter-size planets but also whether they possess rings, moons, or Earth-size companions (*SN*: 7/14/07, p. 24).

The Stardust mission, which early in 2006 dispatched to Earth material that it collected from the shroud of Comet Wild 2, also has a new assignment. In 2011, the craft will fly past Deep Impact's old target, Tempel 1. Stardust will look for changes in the comet's nucleus since the body's last close passage to the sun. —R.C.

ENVIRONMENT

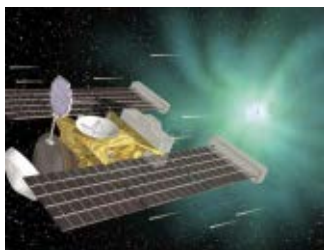
Cholesterol boosts diesel toxicity

Cholesterol poses a cardiovascular risk once it becomes transformed into an inflammatory building block of artery-clogging plaque. That process, which happens all the time, is triggered by oxidation. A new study finds that breathing nanoscale particles spewed by diesel-fuel combustion—also a common occurrence—may turn on genes that multiply

cholesterol's inflammatory and atherosclerotic risks.

André Nel of the David Geffen School of Medicine at the University of California, Los Angeles and his colleagues subjected cells from the lining of human arteries to oxidized cholesterol or diesel particulates. Some 2,500 genes changed their activity in response to both insults. Among this group, the researchers discerned what Nel calls "a genetic footprint" of heightened activity by genes whose activity promotes inflammation.

Pairing a low concentration of diesel particles with a high concentration of oxidized cholesterol ratcheted up the unwanted activity of some of these genes to 15 times the activity triggered by either of the agents alone.



NEW JOURNEY The Stardust mission, which collected material from Comet Wild 2 in 2004, is now scheduled to visit Comet Tempel 1 in 2011.

Nel's team reports similar genetic changes in mice engineered to develop high cholesterol, when they were exposed to Los Angeles traffic for 5 hours per day, 3 days a week, for 2 months.

The findings appear in the July 26 *Genome Biology*.

People who eat fatty foods or who have a genetic predisposition to high cholesterol can't completely avoid air pollution's

exacerbating impacts by moving to remote areas. "You probably will be exposed to far more ultrafine [combustion] particles in Los Angeles," Nel says, but emerging data show that once emitted, such particles travel long distances—even across oceans. In other words, he notes, "they're everywhere." —J.R.

ANIMAL SCIENCE

Gender bender

Call the gender police. Girl mice act like frisky boys when a chemical-sniffing organ crucial for courting behavior is disabled.

The altered females chased cage mates of both sexes, persistently sniffing their rear ends, mounting them, and emitting high-frequency cries typical of mating males. "The females behave exactly like the males," says Catherine Dulac of the Howard Hughes Medical Institute and Harvard University.

Dulac prompted the gender bending by disabling a key gene in the vomeronasal organ, also called Jacobson's organ. This slice of tissue sits deep in the nasal cavity, where it senses the chemical messengers called pheromones when they're released by other mice.

The unexpected behavioral switch occurred in female mice engineered to lack a gene called *Trpc2*. Surprisingly, the researchers found that surgically disabling the vomeronasal organ caused genetically normal adult females to exhibit the same suite of randy behaviors.

The findings suggest that adult female mice possess a "perfectly functional male-behavior circuit," Dulac says.

The females, which subsequently all became pregnant during their sexually voracious encounters, neglected child-care duties, eventually abandoning their offspring.

The researchers caution that their findings do not extend to people. People lack the vomeronasal organ, relying instead on visual and behavioral cues to distinguish boys from girls.

The findings were reported online Aug. 5 in *Nature*. —B.V.

HEALTH PHYSICS

CT heart scans: Risk climbs as age at screening falls

Use of computed tomography (CT) scans to investigate heart blockages is becoming common, especially for people entering emergency rooms with severe chest pain. A new study quantifies a downside to these rapid and relatively noninvasive scans: Their X rays can substantially increase an individual's cancer risk. Younger patients, especially women, incur the greatest increases.

Andrew J. Einstein of Columbia University Medical Center and his colleagues employed computer modeling to calculate radiation exposures to organs as would occur during CT scanning of a man's or woman's heart. The researchers then estimated the likelihood that these phantom organs would develop cancer. They did this by comparing the estimated X-ray doses to those corresponding to age- and gender-adjusted cancer risks in the National Academy of Sciences' most recent report on radiation effects.

Among the men, the team concludes, each scan at age 20 increases the lifetime chance of developing cancer by 1 in 686. The extra lifetime-cancer risk from a scan of an 80-year-old man would be 1 in 3,261. By contrast, a 20-year-old woman's extra cancer risk from a scan is probably 1 in 143, and an 80-old-woman would gain a 1 in 1,338 risk of cancer from a CT heart scan. The researchers report their calculations in the July 18 *Journal of the American Medical Association*.

Younger patients may experience greater risks because precancerous changes in their tissues have more time to mature, Einstein says. Moreover, he notes, breast tissue—heavily exposed in these scans—is more radiation sensitive in women than in men.

The findings, Einstein concludes, suggest that CT scans should be largely restricted to older patients at high risk of heart disease. —J.R.

MATERIALS SCIENCE

Pliable carbon

Researchers have made graphene paper. Graphene is the net of carbon atoms, reminiscent of chicken wire, that forms graphite and carbon nanotubes.

In graphite, electrostatic forces make graphene layers cling together and form microscopic stacks, says Rodney Ruoff, a physical chemist at Northwestern University in Evanston, Ill. Different stacks don't stick together well, which is why pencil lead is soft. But a graphene layer itself is one of the strongest materials in nature, Ruoff says.

Ruoff's team sought to take the layers apart and reassemble them in a new way. The researchers oxidized graphite and shook it in water, producing a suspension of graphene fragments up to 1 micron wide in which about every other carbon atom was strongly bonded to an oxygen atom.

After most of the water has been filtered out, the fragments stuck together to create a new material in the form of a pliable sheet. Remaining water molecules held graphene layers less than a nanometer apart, the team reports in the July 26 *Nature*. "Water is playing the role of a sort of molecular glue," Ruoff says.

The graphene paper is about as strong as aluminum foil, but Ruoff says that replacing water with better molecular glues could lead to new, superstrong materials. —D.C.

ASTRONOMY

Veiled black holes

Lurking at the centers of many galaxies, supermassive black holes make their presence known by gobbling gas, which heats up to fuel quasars and other fireworks. These so-called active galactic nuclei (AGN) are among the most luminous objects in the universe. Now astronomers say that they've found a new, relatively common class of AGN, so heavily smothered

by gas and dust that virtually none of the visible and ultraviolet light generated within them can get out.

These hidden AGN came to light over the past 2 years, when the Earth-orbiting Swift spacecraft detected high-energy X rays coming from the cores of several hundred otherwise unremarkable galaxies. The X rays can pass unimpeded through thick blankets of gas and dust that block lower-energy radiation. Jack Tueller of NASA's Goddard Space Flight Center in Greenbelt, Md., and his colleagues then studied two of these AGN with Suzaku, a Japanese-U.S. X-ray mission.

Although it records X rays over a much broader range of energies than Swift can, Suzaku found little medium and low-energy X-ray emission, which may explain why previous searches hadn't found these AGN. In the leading model of AGN, a supermassive black hole is encircled by a doughnut of gas and dust. An observer looking directly down the hole has a clearer view of the activity within than an observer who looks through the doughnut. But in the case of the hidden AGN, the astronomers propose, the entire doughnut is further hidden by a giant cloud of gas and dust.

This new type of AGN could account for up to 20 percent of the X-ray point sources in the sky, Tueller's team estimates in the Aug. 1 *Astrophysical Journal Letters*. —R.C.

ENVIRONMENT

Beware summer radon-test results

Measuring radon with testing kits that sit in a house for just a few days can yield misleadingly low values in summer, a new study finds.

Alabama maintains a statewide database of 36,000 domestic measurements of radon, a radioactive gas emitted by rocks in soil. Although these data revealed some geographical hot spots, radon readings in such areas were often unexpectedly low if testing had occurred in summer.

To investigate a possible seasonal bias, James L. McNees of the Alabama Department of Public Health in Montgomery and Susan H. Roberts of the Alabama Radon Education Program at Auburn University offered free radon-test kits to state residents whose homes had recently undergone summer testing.

Of the 186 homes resampled in winter, 63 percent exhibited higher radon values

than they had in summer. Indeed, 27 percent of these homes revealed air concentrations more than five times the 4-picouries-per-liter federal guideline for taking remedial action.

The researchers report their findings in the July *Health Physics*.

The Environmental Protection Agency recommends measuring radon over an entire year. However, because many people test for radon only when they put their homes on the market, several-day testing has become common.

McNees and Roberts suspect that the summer-

radon effect traces to fairly constant temperatures in air-conditioned homes. Normally, they say, temperature differentials would prompt warmer air to rise into the attic, drawing radon-laden air into the home from the soil below it. —J.R.

BIOMEDICINE

Serotonin lower in shift workers

Workers who rotate between day and night shifts are at high risk for sleep and mood disorders. New research highlights a possible biological explanation—lower amounts of the key brain chemical serotonin.

Serotonin helps regulate the brain's circadian cycle and also plays a large role in mood. Antidepressants such as fluoxetine (Prozac) and sertraline (Zoloft) increase production of serotonin that the brain's nerve cells use to communicate.

Silvia Sookoian and her colleagues at the University of Buenos Aires in Argentina drew blood from 437 men who worked only the day shift at a local factory and 246 men who rotated shifts. The team found lower amounts of serotonin and a key serotonin breakdown product in the shift workers. While the difference in serotonin wasn't dramatic, it was statistically significant, the researchers report in the Aug. 1 *Sleep*. They say that it might explain why some shift workers have difficulty adjusting to a rotating schedule.

In 2005, the drug company Cephalon of Frazer, Pa., received Food and Drug Administration approval to market modafinil (Provigil), a medication that works in an unknown way, for "shift work sleep disorder." The company says that the condition is marked by excessive sleepiness, headaches, a lack of focus, and trouble sleeping after work. Cephalon claims that 25 percent of the 6 million people in the United States who regularly or occasionally work nights suffer from the disorder. —B.V.



GALACTIC BLANKET Active galactic nucleus shrouded by gas and dust.

Books

A selection of new and notable books of scientific interest

THE ZEN OF FISH: The Story of Sushi, from Samurai to Supermarket

TREVOR CORSON

Sushi has overcome its modest origins. What began as a cheap Japanese street food has become a staple in supermarkets and restaurants across the United States. Corson, a journalist fluent in Japanese, profiles the history of this culinary treat, mixing cultural history, anecdote, and biology. He tells part of his tale through the eyes of a student enrolled in a sushi-chef training program in Los Angeles. Readers learn that

mold, which is present in miso, soy sauce, and rice vinegar, is an essential ingredient of sushi. The word *sushi*, Corson explains, refers to the rice, not to the fish. The Japanese added rice to sushi simply as a means to preserve the fish; originally, the rice was thrown away before the fish was consumed. Corson chronicles the introduction of sushi to the United States in the early 1970s and presents details about sushi ingredients, such as mackerel, shrimp, and wasabi. He ends with a primer on the proper technique for eating sushi. **HarperCollins, 2007, 372 p., hardcover, \$24.95.**

ENDLESS UNIVERSE: Beyond the Big Bang

PAUL J. STEINHARDT AND NEIL TUROK

The Big Bang theory posits that the universe sprang into being in a violent explosion more than 14 billion years ago. In recent decades, the theory has been revised on the basis of information that astronomers

have gleaned from their ongoing observations of the skies as well as of new findings relating to the apparent acceleration of the universe's expansion. In this book, leading cosmologists Steinhardt and Turok propose a provocative alternative theory to the Big Bang. They suggest that time and space didn't begin with a single, cata-

clysmic explosion. On the contrary, the Big Bang was simply one event in a cycle of creation; it occurred as the result of a collision of this universe with a parallel one. They suggest that their theory addresses some of the flaws in the inflationary model of the universe and explain how theorists are using particle physics and string theory to model the new, cyclic model of the universe's origins. The authors outline each theory and provide evidence to support what it proposes about the universe. **Doubleday, 2007, 284 p., b&w illus., hardcover, \$24.95.**

AN OCEAN OF AIR: Why the Wind Blows and Other Mysteries of the Atmosphere

GABRIELLE WALKER

Air may be Earth's most underappreciated resource. Indeed, Earth's atmosphere makes life possible—it is essential to the food people eat, warms the surfaces they walk on, provides a constant supply of

oxygen, allows radio waves to transmit information around the globe, and protects all living things from the effects of solar flares and radiation. Walker, a science writer, gives due attention not only to the planet's ocean of air but also to scientists who have made vital discoveries about it. For instance, the Italian mathematician Evangelista Torricelli was the first to measure the weight of the atmosphere.

Frenchman Antoine Lavoisier discovered the life-giving oxygen in air, and scientists used information from 19th-century theorist Svante Arrhenius to demonstrate how carbon dioxide traps heat in the atmosphere. Walker describes how air moves around Earth and supports aircraft and how solar flares interact with Earth's atmosphere to create breathtaking auroras.

Harcourt, 2007, 272 p., hardcover, \$25.00.

THE HAZARDS OF SPACE TRAVEL: A Tourist's Guide

NEIL F. COMINS

Space tourism is becoming an increasingly realistic possibility, at least for those able to afford the hefty ticket prices. Lest everyone jump on the space

bandwagon prematurely, Comins offers this cautionary tale describing some of the dangers that interplanetary tourists are likely to face. Beyond the International Space Station, which has already been host to space tourists, Comins lists other possible space destinations, from suborbital flights taken to experience

weightlessness to 5-year-long trips to Jupiter. Comins outlines the risks associated with artificial atmospheres within spacecraft and spacesuits. He describes the atmospheric conditions on Mars and the dangers of space dust. Other hazards include collisions with space debris and meteorites, the effects of low gravity on the human body, and the psychological stresses of living in close quarters with other people. Even the most motivated would-be space tourist may think twice after reading this book. **Villard Books, 2007, 253 p., b&w photos and illus., hardcover, \$19.95.**

THE WORLD WITHOUT US

ALAN WEISMAN

What would happen to the world if humans were to suddenly disappear? This provocative question provides the impetus for this book, which looks at how humans have changed the planet and explores whether monuments, artworks, plastics, and other

by-products of civilization would remain as evidence of human existence. Science writer Weisman travels around the world, pondering what Earth was like before the appearance of humans. He interviews dozens of experts who speculate on how the planet would fare without humans. In some areas, crops

would grow to Amazonian proportions, while other areas would remain barren. Many of our landfills would be immune to decomposition. Some animals would flourish, but others, which have come to rely on people for their survival, would mourn humankind's passing. **St. Martin's, 2007, 324 p., b&w illus., hardcover, \$24.95.**

LETTERS

Sum kids

While testing was done on 5- or 6-year-old children ("Take a Number: Kids show math insights without instruction," *SN*: 6/2/07, p. 341), it would be interesting to see if this intuitive skill persists after these students are exposed to standard mathematical instruction in the higher grades. I suspect that the answer will be no, as students restricted to a method of learning math will be deprived of this original ability.

NELSON MARANS, SILVER SPRING, MD.

The pictorial examples presented suggest a possible problem with the design of the study or the need for a reinterpretation of the results. In both examples, the correct answer corresponds to the picture of Sarah, who has two bags above her image. Two bags would correspond to "more" in most kids' minds, regardless of the numerical labeling and mathematical operation depicted and whether or not the kids can understand numerical and mathematical representation. I am suspicious of the results of the study.

KEITH PROPP, COLORADO SPRINGS, COLO.

Having been an early childhood educator for a number of years, I have a concern after reviewing the examples you gave. My experience working with young children has been that they will say whichever example has the most objects is worth "more." Example: When learning about money, the students would often say that a child with three pennies has "more" money than a child with one nickel.

DALE FISHEL, INDIANAPOLIS, IND.

Blowback

People get excited about the birds and bats killed by 400-foot windmills planted in their flyways ("Guidelines for wind farms," *SN*: 6/9/07, p. 365), but the average wind speed should also be considered. In our region, the wind speed averages 11 to 12 miles per hour, but the windmills are most efficient where winds are 30 mph. Unfortunately, many regions with good wind speeds don't have the infrastructure to transport electricity, and the wind-factory people don't want to cut their profits to build them. It seems a shame to lose good agricultural land to a second-rate energy system.

MARGARET DELFELD, BROWNSVILLE, WIS.

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