

## Program Allows Virtual Tour of Ancient Roman Cologne

**A team of archaeologists, scientists and software programmers has created a 3D virtual model of the city of Cologne as it was 2,000 years ago. Though not yet online, the software allows visitors to fly through the city in its Roman glory.**

A new computer program will allow the curious to see Cologne, Germany's fourth-largest city, as it was almost 2,000 years ago, when it was a major northern outpost of the Roman Empire.

"Now, for the first time, people will be able to visualize what an amazing city Cologne already was in antiquity," said Hansgerd Hellenkemper, the director of the city's Romano-Germanic Museum.

The city's history stretches back to 38 B.C. After Julius Caesar pushed the empire north during his conquest of Gaul in the mid-first century B.C., the Romans resettled the Germanic Ubii tribe on the banks of the Rhine River. In 50 A.D., the settlement was granted the status of an official Roman city and was given the name Colonia Claudia Ara Agrippinensium. The city grew to be a major trading center, a status it still preserves today.

The program allows visitors to use a computer mouse to navigate a virtual "flight" around the city, where they will find impressive sights, such as the massive city wall and its monumental gates, the forum, the over 40-meter-high (130-foot) Capitoline Temple, the forum with its semicircular portico and the proconsul's palace.

The project, which has taken over three years to put together, is a collaboration between archaeologists, researchers and software experts drawn from the Archaeology Institute at the University of Cologne, the Köln International School of Design (KISD), the Cologne University of Applied Sciences, the University of Potsdam's Hasso Plattner Institute (HPI) and Cologne's Romano-Germanic Museum.

According to the project's Web site, the purpose of creating the model was to "allow Roman Cologne to be visualized using the findings of current research and to thereby make it comprehensible in its historical dimension to an even larger public."

While the model's content was completed this week and can be accessed using CAD software, it has yet to be made accessible online. The project's leaders have declined to specify when this process will be completed, but the project's team has already begun working on its next project, a virtual model of modern Cologne, dominated by the 157-meter (515-foot) twin spires of its famous cathedral.



Click on a picture to launch the image gallery (6 Photos)



Foto: Hasso-Plattner-Institut

Hamburg and Berlin already have 3D city models that allow users to take virtual flights through the cities using Google Earth. Virtual models of other historical places also exist -- for example, for Rome, Pompeii and Herculaneum -- but in a different form. "Those were more like computer-generated animations rather than large-scale models that you could navigate," says Jürgen Döllner, a professor of computer graphics at the HPI, who led the technical implementation of the project. *jt* -- with wire reports

## Doctors get death diagnosis tips

Doctors are being given tips to help them diagnose when someone is dead.

Although a patient coming back from the dead is rare, there is enough ambiguity in diagnosing death that doctors need guidance, experts have decided.

Rapid advances in life support, where machines take over the breathing of the moribund, have complicated the diagnosis, for example. The Academy of Medical Royal Colleges' UK guidelines cover situations like hypothermia and drug-induced coma.

### Back from the dead

There have been instances when people exposed to extreme cold have been presumed dead but have later shown signs of life again when their core body temperature has risen again.

Sedative drugs can also make a person appear to be dead when they are not.

The report's author, anaesthetist Sir Peter Simpson, said diagnosing death could be difficult.

"There are issues when people die in unusual circumstances with unusual sedative drugs on board or other extraneous things like low body temperature when it is inappropriate to confirm death.

"This new guidance for the first time clearly spells out when it is appropriate to diagnose death.

"Diagnosing death in whatever circumstances is a sensitive issue, which comes at a very distressing time for everyone. "We hope that the detailed way in which the working party has addressed the issues will give help and confidence to all concerned."

The guidelines say the definition of death should be regarded as the irreversible loss of the capacity for consciousness, combined with irreversible loss of the capacity to breathe.

They replace existing guidance on brain death and include new advice on cardiac death.

The authors also decided it was important to separate completely the diagnosis and confirmation of death from anything to do with the issues surrounding organ donation and transplantation. This was to avoid any concern that the diagnosis is influenced by the desperate need for life-saving donor organs which are in short supply.

Professor Dame Carol Black, chair of the Academy of Medical Royal Colleges, said: "I am confident that by addressing the ambiguities of the old Code, together with issues that have arisen as a result of new areas of clinical practice and the law, this new guidance will help both medical and nursing staff and equally our patients feel confident in the diagnosis and confirmation of death and its consequences."

### **Fatty acids clue to Alzheimer's**

***Controlling the level of a fatty acid in the brain could help treat Alzheimer's disease, an American study has suggested.***

Tests on mice showed that reducing excess levels of the acid lessened animals' memory problems and behavioural changes.

Writing in *Nature Neuroscience*, the team said fatty acid levels could be controlled through diet or drugs.

A UK Alzheimer's expert called the work "robust and exciting".

There are currently 700,000 people living with dementia in the UK, but that number is forecast to double within a generation.

#### **Over-stimulation**

Scientists from Gladstone Institute of Neurological Disease and the University of California looked at fatty acids in the brains of normal mice and compared them with those in mice genetically engineered to have an Alzheimer's-like condition.

They identified raised levels of a fatty acid called arachidonic acid in the brains of the Alzheimer's mice.

Its release is controlled by the PLA2 enzyme.

The scientists again used genetic engineering to lower PLA2 levels in the animals, and found that even a partial reduction halted memory deterioration and other impairments.

Dr Rene Sanchez-Mejia, who worked on the study, said: "The most striking change we discovered in the Alzheimer's mice was an increase in arachidonic acid and related metabolites [products] in the hippocampus, a memory centre that is affected early and severely by Alzheimer's disease."

He suggested too much arachidonic acid might over-stimulate brain cells, and that lowering levels allowed them to function normally.

Dr Lennart Mucke, who led the research, added: "In general, fatty acid levels can be regulated by diet or drugs.

"Our results have important therapeutic implications because they suggest that inhibition of PLA2 activity might help prevent neurological impairments in Alzheimer's disease.

"But a lot more work needs to be done before this novel therapeutic strategy can be tested on humans."

#### **'Cautious optimism'**

Rebecca Wood, chief executive of the UK's Alzheimer's Research Trust, said: "This research on mice suggests a connection between fatty acids and the abnormal brain activity that exists in Alzheimer's disease.

"This is cause for cautious optimism, as fatty acid levels can be controlled to some extent by diet and drugs.

"However, it is not yet clear if these findings are applicable to humans, and a lot more research is needed before any human trials can be conducted."

Professor Clive Ballard, director of Research at the Alzheimer's Society, said the work was "robust and exciting". He added: "This is a novel and potentially exciting area of research, but it is still at a very early stage. "Much more research is needed to see if fatty acids could lead to a treatment for those living with the devastating effects of Alzheimer's disease."

### **Study examines link between beta-blocker use and risks of death and heart attack after surgery**

Some patients who received beta-blockers before and around the time of undergoing non-cardiac surgery appear to have higher rates of heart attack and death within 30 days of their surgery, according to a report in the October issue of *Archives of Surgery*, one of the JAMA/Archives journals.

Non-cardiac surgery carries a risk of death, stroke or heart attack in patients who have or are at risk for heart disease, according to background information in the article. "Prevention of these perioperative [around the time of surgery] cardiac complications continues to be the goal of intense research and investigations," the authors write. Following observations of an increase in heart rate before such events and clinical reports of fewer

complications in patients taking beta-blockers for hypertension, researchers began investigating whether these medications should be given to patients undergoing surgery.

Haytham M. A. Kaafarani, M.D., of the Veterans Affairs Boston Health Care System, Boston University and Harvard Medical School, Boston, and colleagues examined 1,238 patients who underwent non-cardiac surgery—including plastic, vascular, abdominal or hernia repair surgery—at one medical center in 2000. Before their procedures, the patients were classified as high, intermediate, low or negligible cardiac risk, and each procedure was also classified as high-, intermediate- or low-risk. A total of 238 patients received beta-blockers perioperatively and were matched by age, sex, cardiac risk, procedure risk, smoking status and kidney health to 408 patients who also underwent surgery at the same center but did not receive beta-blockers.

"Patients at all levels of cardiac risk who received beta-blockers had lower preoperative and intraoperative heart rates," the authors write. Over the 30 days after surgery, the beta-blocker group had higher rates of heart attack (2.94 percent vs. 0.74 percent) and death (2.52 percent vs. 0.25 percent) than those in the control group.

None of the deaths occurred among patients classified as high cardiac risk. However, those in the beta-blocker group who died had significantly higher heart rates before surgery than those who didn't (86 beats per minute vs. 70 beats per minute). "As subtle as it may be, this finding suggests that a low target preoperative rather than intraoperative heart rate is essential for the protective effect of beta-blockers," the authors write. "The relationship between preoperative (rather than intraoperative or postoperative) heart rate and perioperative mortality stresses the importance of not only initiating but also titrating the effect of beta-blockers to an acceptable target heart rate before surgery."

"In summary, our study adds to the controversy regarding the optimal use of perioperative beta-blockers in patient populations at various levels of cardiac risk," the authors write. "Further investigations in this field with standardizing of beta-blockade regimen and with monitoring of heart rate in populations at various levels of cardiac risk should be pursued."

*(Arch Surg. 2008;143[10]:940-944. Available pre-embargo to the media at [www.jamamedia.org](http://www.jamamedia.org).)*

### **Light-activated therapy may change skin at molecular level**

Photodynamic therapy—which involves a light-activated medication and exposure to a light source—appears to produce changes at the molecular level in aging skin, according to a report in the October issue of Archives of Dermatology, one of the JAMA/Archives journals. These changes are consistent with increased collagen production and improved appearance of the skin.

"The deleterious effects of exposure of the skin to UV irradiation are well established," the authors write as background information in the article. "Alternatively, several visible and infrared lasers and light sources have been reported to produce various positive changes in the clinical and histologic [microscopic] appearance of the skin. In recent years, the concept of employing a photosensitizing compound to enhance the effects of some light-based therapies has been espoused."

For aesthetic treatments, this type of photodynamic therapy typically involves application of a topical medication, such as 5-aminolevulinic acid (5-ALA), that is activated by exposure to light. Jeffrey S. Orringer, M.D., and colleagues at the University of Michigan Medical School, Ann Arbor, studied this treatment in 25 adults age 54 to 83 with sun-damaged skin on their forearms. Before treatment, the degree of skin damage was rated and a biopsy (tissue sample) was taken from the forearm. A solution containing 5-ALA was applied to the treatment site and left on for three hours; the skin was then washed with cleanser and treated with a pulsed-dye laser. Participants returned for re-examination and to provide additional biopsy samples four to five times during the six months following treatment.

After photodynamic therapy, tissue samples demonstrated a five-fold increase in levels of Ki67, a protein thought to play a fundamental role in the growth and development of new skin cells. The epidermis (skin's outer layer) increased in thickness 1.4-fold. Levels of enzymes and other compounds associated with the production of collagen, the main structural protein in the skin, also were increased.

"Photodynamic therapy with the specific treatment regimen employed produces statistically significant quantitative cutaneous molecular changes (e.g., production of types I and III collagen) that are associated with improved appearance of the skin," the authors conclude. When compared with previous data regarding the effectiveness of pulsed-dye laser therapy alone, these results suggest that using a photosensitive compound such as 5-ALA enhances changes in the skin.

"Although our molecular measurements cannot yet precisely predict clinical outcomes for a single given patient, taken together they are very much in keeping with the bulk of the clinical literature and thus lend substantial support to the conclusions reached by other researchers who have published purely clinically oriented work in this field," the authors conclude. "We believe that the quantitative amount of dermal repair and regeneration induced by a specific therapeutic intervention very likely underlies the degree of clinical

rejuvenation produced. Thus, it is our hope that, with further development, our working molecular model may one day be used to predict the clinical value of new technologies in aesthetic dermatology."

(*Arch Dermatol.* 2008;144[10]:1296-1302. Available pre-embargo to the media at [www.jamamedia.org](http://www.jamamedia.org).)

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### **'A dinosaur dance floor'**

#### **Numerous tracks at Jurassic oasis on Arizona-Utah border**

SALT LAKE CITY – University of Utah geologists identified an amazing concentration of dinosaur footprints that they call "a dinosaur dance floor," located in a wilderness on the Arizona-Utah border where there was a sandy desert oasis 190 million years ago.

The three-quarter-acre site – which includes rare dinosaur tail-drag marks – provides more evidence there were wet intervals during the Early Jurassic Period, when the U.S. Southwest was covered with a field of sand dunes larger than the Sahara Desert.

Located within the Vermilion Cliffs National Monument, the "trample surface" (or "trampled surface") has more than 1,000 and perhaps thousands of dinosaur tracks, averaging a dozen per square yard in places. The tracks once were thought to be potholes formed by erosion. The site is so dense with dinosaur tracks that it reminds geologists of a popular arcade game in which participants dance on illuminated, moving footprints.



*Geologist Winston Seiler with some of the dinosaur tracks he identified for his thesis as a University of Utah master's degree student. The impressions once were thought to be potholes eroded by water. But Seiler and Marjorie Chan, chair of geology and geophysics at the University of Utah, published a scientific paper in the October 2008 issue of the journal Palaios identifying the abundant impressions as comprising a large dinosaur "trample surface" in northern Arizona. There are so many tracks they wryly refer to the site as "a dinosaur dance floor."* Nicole Miller

"Get out there and try stepping in their footsteps, and you feel like you are playing the game 'Dance Dance Revolution' that teenagers dance on," says Marjorie Chan, professor and chair of geology and geophysics at the University of Utah. "This kind of reminded me of that – a dinosaur dance floor – because there are so many tracks and a variety of different tracks."

"There must have been more than one kind of dinosaur there," she adds. "It was a place that attracted a crowd, kind of like a dance floor."

A study identifying the dinosaur track site was published in the October issue of the international paleontology journal *Palaios*. Chan is senior author of the study, which was conducted for a master's degree thesis by former graduate student Winston Seiler, who now works at Chevron Inc., in Bakersfield, Calif.

Seiler says the range of track shapes and sizes reveals at least four dinosaur species gathered at the watering hole, with the animals ranging from adults to youngsters.

"The different size tracks [1 inch to 20 inches long] may tell us that we are seeing mothers walking around with babies," he says.

The site – a 6-mile roundtrip hike from the nearest road – is in Arizona in the Coyote Buttes North area of the Paria Canyon-Vermilion Cliffs Wilderness, which is part of the U.S. Bureau of Land Management's (BLM) Vermilion Cliffs National Monument. The track site – about halfway between Kanab, Utah, and Page, Ariz. – is near a popular wind-sculpted sandstone attraction known as the Wave.

#### **A Dense Collection of Dinosaur Footprints – and a Few Tail Drags**

Chan says the new study is the first scientific publication to identify the impressions as dinosaur footprints on a trample surface.

As part of the study, Seiler marked off 10 random plots, each of 4 square meters, or roughly 2 yards by 2 yards. He counted 473 tracks within those plots – an average of 12 per square meter. He conservatively estimates the 3,000-square-meter site (about 0.75 acres) has more than 1,000 tracks, but he and Chan believe there perhaps are thousands.

Numerous dinosaur track sites have been found in the western United States, including more than 60 in Navajo Sandstone, where actual dinosaur bones are rare.

"Unlike other trackways that may have several to dozens of footprint impressions, this particular surface has more than 1,000," Seiler and Chan wrote. And they say the density of tracks is much greater than it is at even larger track sites, such as the one at Coral Pink Sand Dunes State Park in Utah.

The dinosaur tracks and tail marks near the Wave were preserved in the vast Navajo Sandstone Formation. But unlike the dunes that make up much of the Navajo Sandstone, the tracks are within what was a wet, low watering hole between the dunes.

"We're looking at an area much like the Sahara Desert with blowing sand dunes," Seiler says. "Areas between these sand dunes could have had ponds – oases."

The 2.4-inch-wide tail-drag marks – which are up to 24 feet long – are a special discovery because there are fewer than a dozen dinosaur tail-drag sites worldwide, Seiler says. Four tail drags were within the 10 plots he surveyed, and there are others nearby.

"Dinosaurs usually weren't walking around with their tails dragging," he says.

### **Potholes – or Prints from Four Kinds of Dinosaurs?**

Chan first visited the site of the dinosaur tracks in 2005 with a BLM ranger who was puzzled by them. Chan initially called them potholes, which are erosion features common in desert sandstone, "but I knew that wasn't the whole story because of the high concentration and because they weren't anywhere else nearby but along that one surface."

Seiler first saw the site in 2006. "At first glance, they look like weathering pits – a field of odd potholes," he says. "But within about five minutes of wandering around, I realized these were dinosaur footprints."

One anonymous reviewer of the Palaios study still believes the holes are erosion features. The study argues the impressions are from dinosaurs because:

- \* They are the correct size for tracks made by big animals, and are limited to a single rock bed.

- \* Four different kinds of footprint shapes are seen repeatedly in 14 percent of the impressions, and they include obvious claw, toe and heel marks. The other impressions "are clearly similar."

- \* One-third of the prints are surrounded by small ridges or mounds. Such features would be expected when animals stepped in wet sand.

- \* The tracks "are rarely flat and are typically oriented at an angle into the sediment ... and indicate a clear direction of travel" to the west-southwest. Seiler says the direction the dinosaurs walked "either was dictated by the large dunes that bounded this wet area, or it could be communal behavior, like walking together as a pack."

- \* About one-eighth of the tracks show "overprinting," in which a dinosaur stepped in the footprint of another or even in its own prints.

"While these impressions may be mistaken for potholes caused by weathering, close examination reveals many footprint features," Seiler says.

Dinosaur footprints are named by their shape because the animals that made them haven't been identified. Four kinds of footprints were found on the trample surface:

**Eubrontes** footprints measure 10 inches to 16 inches long and have three toes and a heel. Eubrontes tracks are believed to have been made by upright-walking dinosaurs 16 to 20 feet long, or smaller than *Tyrannosaurus rex*.

**Grallator** tracks are about 4 inches to 7 inches long, are three-toed and were left by small dinosaurs only a few feet tall.

**Sauropodomorph** dinosaur tracks, which are more circular than the other types, were left by creatures that walked on four legs and were the largest dinosaurs at the site. Their tracks range from 6 inches to 11 inches long. Seiler says the tail-drag marks are associated with these circular footprints, so they likely were made by sauropods.

**Anchisauripus** tracks measure 7 inches to 10 inches long and were made by dinosaurs that ranged from 6 feet to 13 feet in length.

*This Eubrontes dinosaur footprint -- including three toes and a heel -- measures roughly 16 inches long. Dinosaur footprints are named by their shape because the species and genus of animal that made them isn't known, although Eubrontes tracks are believed to have been made by upright-walking, meat-eaters smaller than Tyrannosaurus rex. Eubrontes is one of four types of dinosaur footprints identified by University of Utah geologists at a Jurassic Period dinosaur "trample surface" in northern Arizona. The footprint previously had been thought to be modern potholes eroded by water. The inset outlines the footprint shape.* Winston Seiler, University of Utah



### **An Oasis for Dinosaurs in a Vast Desert of Dunes**

When the footprints were made 190 million years ago, "the continents were arranged so this area was in the tropics" and was part of the supercontinent named Pangaea, says Seiler. "It was a desert, like the Sahara but much larger than the Sahara is today," covering much of Utah, Wyoming, Colorado, New Mexico, Arizona and Nevada.

"Some studies indicate winds probably were much stronger than normal because all the continents were together," says Chan. "That's why you had monster dunes."

"To support large dinosaurs, there probably wasn't just one watering hole for them to go to, but many," Seiler says. "They wandered between a network of watering holes for food and water."

In that sense, the trample surface is not "just a wet pond," but "it's possibly a record of global climate change" – a shift from drier to wetter conditions, Chan says.

She says the traditional view is that the Navajo Sandstone represents "a vast, dry uninhabitable desert. But now we are seeing there are a lot of variations, and there were periods when dinosaurs were living there." Seiler envisions the dinosaurs were "happy to be at this place, having wandered up and down many a sand dune, exhausted from the heat and the blowing sand, relieved and happy to come to a place where there was water."

The trample surface "helps paint a picture of what it was like to live back then," he says. "Tracks tell us what the dinosaurs were doing, what their behavior was, what life was like for them, what they did on a day-to-day basis."

After the dinosaurs left their prints, the trample surface was covered by shifting dunes, which eventually became Navajo Sandstone. Then, the rock slowly eroded away, exposing the tracks. The tracks eventually will erode too, Seiler says.

### **Blue Bananas**

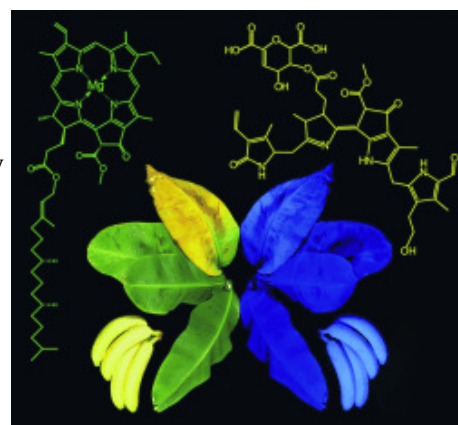
#### ***Ripening bananas glow an intense blue under black light***

Ripe bananas are of course yellow. However, under black light, the yellow bananas are bright blue, as discovered by scientists at the University of Innsbruck (Austria) and Columbia University (New York, USA). The team, headed by Bernhard Kräutler, reports in the journal *Angewandte Chemie* that the blue glow is connected to the degradation of chlorophyll that occurs during ripening. In this process, colorless but fluorescing breakdown products of chlorophyll are concentrated in the banana peel.

The usual appearance of bananas is mainly the result of carotenoids. Under normal light, these natural pigments appear yellow. Under UV light, known to partygoers as black light, ripening bananas appear blue instead. There is no difference between naturally ripened bananas and those ripened with the use of ethylene gas. Green, unripe bananas do not fluoresce. The intensity of the luminescence correlates with the breakdown of the green pigment chlorophyll. As the ripening continues to progress, the blue glow decreases. "Surprisingly, this blue luminescence apparently has been entirely overlooked," says Kräutler.

By means of various spectroscopic techniques, the team analyzed the structure of the main breakdown products. In doing this, they identified a propionate ester group, a modification never seen before in a chlorophyll breakdown product. This group has a stabilizing effect and could explain the unusually long duration of the fluorescing intermediates in bananas. Fluorescing chlorophyll catabolytes have otherwise only been found as short-lived intermediate products in higher plants.

Why does the breakdown of chlorophyll occur differently in bananas than in other higher plants, including even banana leaves? Kräutler suggests two different explanations: "In contrast to humans, many of the animals that eat bananas can see light in the UV range. The blue luminescence of the banana fruit could give them a distinct signal that the fruit is ripe." Or perhaps the chlorophyll degradation products also serve a biological function for the banana. The amazingly stable catabolytes could help to prolong the viability of the ripening fruit.



### **Study finds creating unique health ID numbers would improve health care quality, efficiency**

Creating a unique patient identification number for every person in the United States would facilitate a reduction in medical errors, simplify the use of electronic medical records, increase overall efficiency and help protect patient privacy, according to a new RAND Corporation study.

Although creating such an identification system could cost as much as \$11 billion, the effort would likely return even more in benefits to the nation's health care system, according to researchers from RAND Health.

"Establishing a system of unique patient identification numbers would help the nation to enjoy the full benefits of electronic medical records and improve the quality of medical care," said Richard Hillestad, the study's lead author and a senior principal researcher at RAND, a nonprofit research organization. "The alternative is to rely on a system that produces too many errors and puts patients' privacy at risk."

Federal legislation passed over a decade ago supported the creation of a unique patient identifier system, but privacy and security concerns have stalled efforts to put the proposal into use.

As adoption of health information technology expands nationally and more patient records are computerized, there have been increasing calls to create a system that would make it easier to retrieve records across varying systems such as those used by doctors and hospitals.

RAND researchers examined the costs of creating a unique patient identification system, compared the error rates of such a system and its alternatives, and examined the operational advances and disadvantages of the technology.

The RAND study concluded that one of the primary benefits created by broad adoption of unique patient identifiers would be to eliminate record errors, and help reduce repetitive and unneeded care.

In the absence of unique patient identifiers, most health systems use a technique known as statistical matching that retrieves a patient's medical record by searching for attributes such as name, birth date, address, gender, medical record numbers, and all or part of a person's Social Security Number.

Reviewing past research studies, RAND researchers estimated that statistical matching returns incomplete medical records about 8 percent of the time and exposes patients to privacy risks because a large amount of personal information is exposed to computer systems during a search.

The study also concluded that many of the privacy concerns related to a unique patient identification system could be addressed through the creation and enforcement of laws that severely punish those who misuse information retrieved with a health ID number.

"Our research suggests that it's easier to safeguard patient privacy with a records system that makes use of a unique health ID rather than a system that uses statistical matching," Hillestad said.

One way to deal with privacy concerns might be to allow to people to voluntarily enroll in a unique patient identification system, researchers say. Such an approach would allow a unique health identifier system to demonstrate that it can be used without compromising patient privacy and can be more accurate than current statistical matching systems.

Some proposals have suggested using patients' Social Security Numbers as a medical identifier. But the RAND study found Social Security Numbers are a poor option because they are so widely used and they pose risks of identify theft.

A genuine unique patient identification system would be more secure because it could include safeguards such as check codes that allow numbers to be easily screened for input errors. Such check codes are mathematical combinations of the other digits in the number and are commonly used in other digital IDs such as those in the product bar codes scanned at checkout counters.

*Support for the study was provided by a consortium of health information technology companies. They include Cerner Corporation, CPSI, Intel, IBM, Microsoft, MISYS, Oracle and Siemens.*

*The study, "Identity Crisis: An Examination of the Costs and Benefits of a Unique Patient Identifier for the U.S. Health Care System," is available at [www.rand.org](http://www.rand.org). Other authors of the report are Richard Hillestad, James H. Bigelow, Basit Chaudhry, Paul Dreyer, Michael D. Greenberg, Robin C. Meili, M. Susan Ridgely, Jeff Rothenberg and Roger Taylor.*

### **'Dry cleaning effect' explained by forgetful Yale researcher**

Yale researchers have described how dueling brain systems may explain why you forget to drop off the dry cleaning and may point to ways that substance abusers and people with obsessive compulsive disorder can overcome bad habits.

In Proceedings of the National Academy of Sciences, Christopher J. Pittenger, M.D., and colleagues describe a sort of competition between areas of the brain involved in learning that results in what Pittenger calls the "dry cleaning effect."

One area of the brain called the striatum helps record cues or landmarks that lead to a familiar destination. It is the area of the commuter's brain that goes on autopilot and allows people to get to work, often with little memory of the trip.

But when driving to an unfamiliar place, the brain recruits a second area called the hippocampus, which is involved in a more flexible system called spatial learning. The commuter must employ this system if he or she wants to run an errand before work.

"When you have driven the same route many times and are doing it on autopilot, it can be really difficult to change," said Pittenger, assistant professor of psychiatry at Yale and senior author the paper. "This is why I cannot, for the life of me, remember to drop off my dry cleaning on the way to work. If I'm not paying enough attention right at that moment, if I am thinking about something else, I just sail right on by."

Pittenger and Yale colleagues Anni S. Lee and Ronald S. Duman developed a way to study how these two modes of learning might be interconnected in mice.

In one group, they disrupted areas of the striatum in mice and discovered that their ability to complete landmark navigation tasks was impaired. However, these mice actually improved on tasks that involved spatial learning.

Conversely, when the researchers disrupted an area of the hippocampus involved in spatial learning, the animals could no longer navigate spatially but learned landmark tasks more quickly.

Pittenger speculates that the interactions between these two systems may be important for understanding certain mental illnesses in which patients have destructive, habit-like patterns of behavior or thought. Obsessive-compulsive disorder, Tourette syndrome, and drug addiction involve abnormal function of the striatum and may also involve disruption of the interactions between the two learning systems, which may make habits stronger and less flexible.

"This is part of what we are doing in cognitive-behavioral therapy when we teach patients to recognize their destructive habits, to take a step back, and to learn to do things differently," Pittenger said. "What we're really asking them to do is to use one of these systems to overcome and, ultimately, to re-train the other."

In time, Pittenger hopes his studies will lead to more effective treatments for psychiatric disease – and, maybe, help him drop off his dry cleaning.

*The research was funded by the National Institute of Health.*

*Citation: Proceedings of the National Academy of Sciences, Oct. 20, 2008*

## **Jupiter produced greatest pounding in Earth's history**

\* 20 October 2008

\* NewScientist.com news service

JUPITER has long been thought to defend the inner planets by kicking dangerous comets and asteroids out into interstellar space. Now it seems the planet could have been responsible for the greatest pounding in Earth's history.

Kevin Grazier of NASA's Jet Propulsion Lab in Pasadena, California, and colleagues built a computer model comprising 40,000 small objects in circular orbits between the outermost planets, similar to the disc of material present in the early solar system. As the simulation progressed, Jupiter hurled over 95 per cent of the objects out of the solar system. But in the process its gravitational tug stretched their circular orbits into loops that crossed the paths of the inner planets.

The model, presented at the Division of Planetary Sciences meeting in Ithaca, New York, this week, provides a possible mechanism for the "late heavy bombardment", a controversial theory which says that some craters on the moon and inner planets were caused by a massive influx of small bodies around 4 billion years ago. The deflection of comets may also explain how volatile substances like water arrived on the inner planets.

The paper ends the myth of a purely protective Jupiter, says Jonathan Horner of the Open University in Milton Keynes, UK. "We're finally making sense of something we should have already known."

### **Really?**

## **The Claim: Coffee Eases Headaches From Epidural Injections**

**By ANAHAD O'CONNOR**

**THE FACTS** Headaches can be an excruciating side effect of routine procedures that involve puncturing the middle and lower back, including spinal taps and anesthetic injections like epidurals.

Doctors and medical texts have long advocated a simple antidote: a cup of Joe. One theory is that the caffeine narrows the cerebral blood vessels, which helps reverse the vasodilation that occurs when a puncture causes cerebrospinal fluid to leak. Research, however, suggests it does not help.



**Leif Parsons**

In 2007, researchers at the Mayo Clinic in Arizona reviewed several randomized studies that looked at caffeine as a treatment for the condition, known as postdural puncture headache, and found no evidence it worked. That echoed the findings of a separate study at the University of California, Los Angeles, and Cedars-Sinai Medical Center in Los Angeles, which found slim evidence supporting caffeine or another popular antidote, more fluid intake.

Other studies suggest that the most effective treatment is one called epidural blood patching. It can be invasive, but it relieves headaches in 85 to 98 percent of patients. It also helps when smaller needles are used. **THE BOTTOM LINE** Studies suggest caffeine is not an effective treatment for headaches caused by lumbar-puncture procedures like epidurals.



## Weight-Loss Surgery, No Cutting Required

By DENISE GRADY

On a recent Wednesday, Karleen Perez lay unconscious on an operating table in Upper Manhattan while her surgeons and two consultants from a medical device company peered at an overhead monitor that displayed images from inside her digestive tract.

The surgeons, Dr. Marc Bessler and Dr. Daniel Davis, had just stapled her stomach to form a thumb-sized tube that would hold only a small amount of food. The operation resembled others done for weight loss, with one huge difference. In Ms. Perez's case, there was no cutting. Instead, the surgeons had passed the stapler down her throat and stapled her stomach from the inside.

Inspecting their handiwork, Dr. Bessler said, "I don't think you'll get much better than that."

The operation, meant to make people feel full after eating very little, is strictly experimental. Only a few patients have tried it in this country, as part of a study paid for by Satiety Inc., which makes the staplers and hopes the Food and Drug Administration will approve them.

Ms. Perez, a 25-year-old graduate student in social work, was the second patient at New York-Presbyterian Hospital/Columbia to enter the study. Satiety employees advised her surgeons throughout the operation.

The procedure is part of a trend to make surgery less painful and invasive, to minimize risks and speed recovery. Many operations that once required big incisions are now performed through small slits, with cameras inserted to let surgeons see what they are doing on video screens. Ms. Perez's doctors took the next step: using a natural opening to avoid cutting through the abdominal wall. Dr. Bessler and other surgeons have used similar techniques to remove the appendix through the mouth, and the gallbladder through the vagina.

In Mexico and Europe over the past two to three years, 98 patients have had the new weight-loss surgery, named Toga (for transoral gastropasty). On average, those who have passed the one-year mark have lost about 40 percent of their excess weight. Only time will tell whether they will be able to avoid gaining it back.

There are older, well-established operations that produce more weight loss, and in the United States 200,000 people have them each year. Known as bariatric surgery, it is often done through slits.

But even the slits leave scars and slice through abdominal muscles, which causes pain, Dr. Bessler said. The operations can have complications, too, like hernias and leaks in the digestive tract. "Most people don't want the risk," he said, adding that only about 2 percent of those who might be helped by bariatric surgery actually have it.

About 15 million Americans are morbidly obese, meaning their body mass index — a type of weight/height ratio — is at least 40 (overweight begins at 25). Medical guidelines recommend surgery when the index reaches 40, or 35 if there are also complications like diabetes or heart disease.

Ms. Perez is 5-foot-9 and weighs 289 pounds, for a body mass index of 42 — though her height and generous frame help hide the weight. Her family, friends and boyfriend say she looks just fine.

But she has mixed feelings about her appearance. She weighed 175 or 180 pounds in high school and was comfortable with that weight. But she gained 90 pounds in college and could not take it off. She hopes the operation will help her lose 60 pounds, maybe even in time for her graduation this coming spring from Stony Brook University.

"I don't feel like it's a big issue, but of course it is," she said. "If I go out with my sorority sisters or friends to buy clothes, I probably can't buy where they do. I'm the one who comes out with accessories. That's a bummer."

More important, she said, is her health. She becomes winded too easily, and her blood pressure "is not great," she said, adding, "I just want to live healthy and not be borderline anything."

Bariatric operations typically work far better than diet, exercise or drugs, and they often cure diabetes and reduce the risk of dying from heart disease or cancer. But there is also a risk — albeit small, less than 1 percent at experienced centers — of dying from the surgery itself.

The idea behind Toga is to offer something safer and less invasive. Dr. Bessler said he thought it would appeal to many people who feared the other operations.

"It has a lot of promise," he said. "I deal with a lot of new technologies. This, I'm really excited about." Dr. Bessler said that he and Dr. Davis had no financial interest in Satiety but that the company did pay for their work on the study.

Other companies are also developing new devices and minimally invasive operations to cash in on America's booming obesity epidemic, but Satiety is among the first to start testing its products in people.

A surgeon not involved in the Toga study, Dr. Philip Schauer, director of bariatric surgery at the Cleveland Clinic, called the new operation very promising and said that so far it seemed to offer "a drastic reduction in side effects and risk."

Though she wanted surgery, Ms. Perez did not want a gastric bypass, the most common bariatric operation, which shrinks the stomach and rearranges the small intestine. Her aunt had it and lost 150 pounds, but suffered from a hernia, intestinal problems and other serious complications.

So Ms. Perez considered gastric banding, a less extreme and increasingly popular operation that inserts a loop around the top of the stomach and tightens it to form a small pouch.

But Toga, which she discovered on the Internet, seemed less invasive. Also, the price was right: the operation would be free as part of the study. She did not mind if it produced less weight loss than the other methods.

“To me, it’s not about being completely skinny,” she said. “I’m told I could lose 40 percent of my excess weight.” If she exercises and diets after the operation, she said, “I’ll probably lose, like, 60 pounds, and that’s realistic to me.”

Temporarily, she kept her plans a secret from most of her friends and impishly told some that she was having her tonsils out. She took down her Facebook page and put a note in MySpace saying that there would be some changes made.

The operation is not as simple as it might sound. To begin, Ms. Perez was given general anesthesia and put on a respirator. Then the surgeons pushed a dilator, a formidable-looking tube about three-quarters of an inch wide, down her throat to stretch her esophagus.

Next came another wide tube, this one about two feet long, containing the stapler. The surgeons inflated her stomach with carbon dioxide to create space in which to work. Dr. Bessler struggled for 5 or 10 minutes to position the stapler properly, and then activated controls that opened it, like a miniature spaceship, inside Ms. Perez’s stomach.

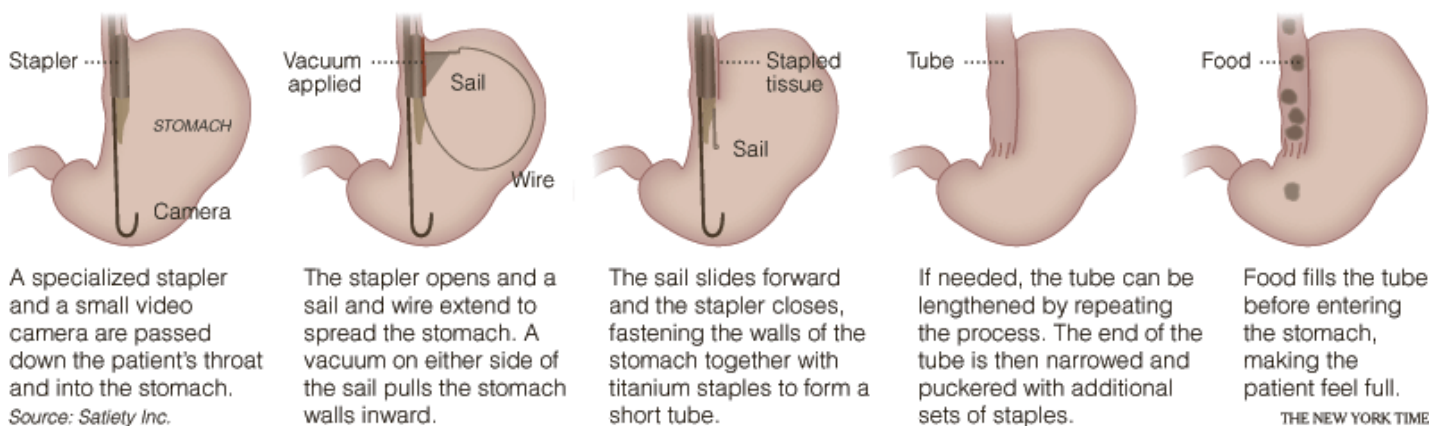
A sail and curving wire emerged from the stapler to help push aside the folds of her stomach. Then Dr. Bessler turned on a vacuum pump to draw parts of the front and back walls of the stomach into the device to be stapled together.

Three rows of staples were needed, but the stapler holds only one row, so the whole apparatus had to be withdrawn, rinsed, reloaded, pushed back down Ms. Perez’s throat and painstakingly repositioned for each row. The Satiety consultants stood close by to coach, at one point warning Dr. Bessler that if he inflated Ms. Perez’s stomach too much, her first row of staples could pop. The surgery took three hours.

“Every operation has its learning curve,” Dr. Bessler said. “We saw a doctor in Brussels who took an hour and a half, but he had done 70.”

### Inside Job

An experimental stomach-stapling operation called Toga, for transoral gastroplasty, avoids cutting through the abdominal wall.



The next morning at the hospital, Ms. Perez was in good spirits despite a horrendous sore throat from the operation. She said she had awakened during the night wondering what she had done, and had thought, “This is going to be super life-changing.”

She would be on a liquid diet for several weeks. A nutritionist had given her a pamphlet that commanded, “Don’t Stretch Your Stomach!,” warned that eating too much or too fast could cause vomiting, and advised that the best time to lose weight would be in the next 6 to 12 months, because the body would try to fight the surgery by absorbing more nutrients.

She thought she could do it. She would start slowly, by taking longer and longer walks. She hoped to join a gym, start running, eventually finish a marathon. She wanted to look cool for her graduation.

“My friends are going to be shocked,” she said. “Through struggle comes success.”

## A Taste for Blood

By NATALIE ANGIER

With his soft voice and friar's manner, Louis Sorkin hardly seems the type to flout the sensible advice of a nursery rhyme. Yet on a recent afternoon at the American Museum of Natural History, Mr. Sorkin, a renowned entomologist, did precisely, luridly that.

He took a glass jar swarming with thousands of hungry specimens of *Cimex lectularius*, better known as bedbugs. The small, roachy-looking bloodsuckers have been spreading through the nation's homes and hotels at such a hyperventilated pace that by next year they are expected to displace cockroaches and termites as America's leading domestic pest insect. To better understand their habits, Mr. Sorkin has cultivated a personal bedbug colony — very personal.



*MEAL PLAN A vampire bat feeding on a donkey in Trinidad. Adrian Warren*

“You see this mesh here?” he said, pointing to a circlet of wiry material taped over the top of his little jam jar of horrors. The weave is dense enough to keep even newborns from escaping, he explained, but porous enough to allow the bedbugs' stylets, their piercing mouthparts, to poke through. Mr. Sorkin pushed up his shirt sleeve and pressed the mesh end of the jar against the inside of his right arm. Roused to a frenzy by the twin cues of heat and carbon dioxide that “in evolution equal host,” said Mr. Sorkin, the insects scrambled toward the lid, thrust out their stylets and began to feed. For a good 10 minutes, Mr. Sorkin sat there with the proud placidity of a donor at a blood bank. He did not budge. He held the jar. He let the bedbugs bite.

“I can hardly feel it,” he said matter-of-factly, “and they do need to eat.”

Mr. Sorkin and his bedbugs are featured in the newly published “Dark Banquet,” a jaunty, instructive and charmingly graphic look at nature's born phlebotomists — creatures from wildly different twigs of the phylogenetic tree that all happen to share a fondness for blood.

The book was written by Bill Schutt, a biologist and bloodsucking aficionado who holds joint positions at the C. W. Post campus of Long Island University and the natural history museum, and that day he, too, was at the museum, to discuss the meal plan variously known as sanguivory and hematophagy, and who does it and when, why and how.

Among his rubied rabble are vampire bats tuned to extract blood from large slumbering mammals and bats that aim instead for the warm breast plates of birds; New World leeches that track their hosts through the water and Old World leeches that relentlessly stalk down blood bearers on land; the notorious vampire finches of the Galápagos that daintily peck open dribbling wounds on the hindquarters of blue-footed boobies; and the candiru, tiny, eel-like catfish that are reputed to have the power to swim up a person's urethra and suck blood from the bladder and thus are often more feared than their fellow river dwellers, the piranhas.

Dr. Schutt, who is waggish and bearded and projects an air of high-voltage goth, also showed off museum specimens of his preferred bloodsuckers, the vampire bats, which in this case were well beyond any need for private Red Cross donations. Yet even post-mortem, the bats' fur felt silky, their wings said da Vinci, and their faces and teeth showed the hallmarks of a wholehearted blood feeder.

As it turns out, the three species of bat that subsist entirely on blood — all of them native to Latin America — are much cuter than the average insect- or fruit-eating bat. Because vampire bats rely as much on heat and odor signals to find their food as they do on echolocation, they have a comparatively modest “nose leaf,” the knobby nasal organ that many bats use to direct their sonar signals and that helps account for the bat's archetypal gargoyle appearance. A vampire bat's incisors and canines are also much sharper and slimmer than standard bat dentition, the better to slip into the flesh of a large mammal or bird without being detected. Then there is the architecture of capillary action. A vampire bat does not suck the blood of its victims but instead lets physics do the sucking, its cleft lower lip, perfectly spaced lower incisors and doubly grooved tongue jointly forming a kind of tube through which a victim's blood is pulled up as readily as water crawls up the stem of a plant.

The bat hastens the capillary action along, explained Dr. Schutt, “by moving its tongue back and forth like a piston.” That fast-flicking tongue also bathes the wound site in a salivary blend of anticoagulants to block blood's natural tendency to clot on exposure. In fact, the anticoagulants in bat spit are so potent that a host animal often continues to bleed long after the vampire bat has feasted its fill and departed.

Dr. Schutt explained that hematophagy is a difficult, dangerous trade, in some ways harder than merely killing and eating your prey outright, which is why blood eaters from different taxonomic orders have evolved a similar set of utensils: the hatpin teeth, the natural clot busters and pain deadeners.

Blood feeders must also be stealthy and wily and good at escaping the swats and fury of their often much larger hosts. The common vampire bat, *Desmodus*, which feeds on large terrestrial mammals, creeps along the ground like a spider and, in addition to flying, can spring straight upward three feet into the air.

The white-winged vampire bat, *Diaemus*, approaches a potential host chicken so softly and lovingly that the bird is deceived and sweeps it up to its brood patch as though to warm its own chick. Aquatic leeches aim for hidden pockets and crevices: dip your head into leech-infested waters, and the segmented, toothy worms may slip up your nostrils and make a home of your nose.

Moreover, even though we rightly cherish our own blood as the indispensable elixir of our lives, it turns out that, as a foodstuff for others, it is surprisingly thin gruel. Blood is more than 95 percent water, with the rest consisting mostly of proteins, a sprinkling of sugars, minerals and other small molecules, but almost no fat. Tiny creatures can do fine on such light fare, which is why the great majority of exclusive blood eaters are arthropods — bedbugs, ticks, chiggers, female mosquitoes. For larger sanguivores, though, it is as much of a challenge to survive on blood as it is to acquire it. Lacking dietary fat, vampire bats cannot pack on adipose stores and must consume the equivalent of half their one-ounce body weight in blood every night or risk starving to death. And because the water in that blood meal would make the bats too heavy to fly, they must cast off all modesty and urinate freely as they feed.

Small wonder that wholehearted exclusive blood feeding is rare among vertebrates, and that two of the three species of vampire bats are found in such low numbers they are at risk of extinction. The only reason that so-called common vampire bats are common, said Dr. Schutt, is that they have learned to feed on cattle, pigs and other livestock. “They love it when we clear out the rain forest to make way for ranches,” he said.

The only other vertebrates known to subsist solely on blood are certain types of candiru, a poorly studied but floridly feared group of inchlong catfish found in the Amazon and Orinoco Rivers. A hematophagous candiru’s usual modus is to parasitize a larger catfish, infiltrating the host’s gill slits, grasping onto the flesh inside, rupturing blood vessels, pumping out the blood with its highly mobile jaws and then, after a minute or two, darting out again. Yet for at least a century, the fish have been reputed to target the human urethra as well, supposedly enticed by the scent of urine: fish, after all, urinate through their gills. Despite the antiquity and persistence of the legend, there is only one confirmed case, from 1997, of a candiru making its way into a human urethra, where it probably had no time for a blood meal before suffocating to death.

Professional blood feeding may not be for the faint of heart, but nature abounds in amateurs and opportunists. The vampire finches of the Galápagos live mostly on seeds, nectar and eggs, but they supplement their diet with occasional high iron snacks, by persistently pecking at the wings and tail region of one of the islands’ well-named blue-footed boobies. Once the finch draws blood, said Dr. Schutt, “you’ll see five finches waiting behind it like customers at a deli counter.”

Another example of a dabbling avian Dracula is the oxpecker, a member of the starling family famed for living aboard large mammals like rhinos, giraffes and buffalo and for plucking the ticks off its carrier’s hide. The oxpecker-mammalian relationship has long been celebrated as a noble case of symbiosis: the piggybacker gets food, the piggybacked gets groomed. More recently, researchers have determined that the oxpeckers do not merely pick off the parasites — they press their beaks in the wounds where the ticks were lodged and take nips of the host mammal’s blood. Who knows whether the poor beast would not rather sleep tight and let a few bugs bite, and instead lose that nasty oxpecker?

### **Study sheds new light on dolphin coordination during predation**

CORVALLIS, Ore. – Spinner dolphins have long been known for their teamwork in capturing prey but a new study using high-tech acoustics has found that their synchronization is even more complex than scientists realized and likely evolved as a strategy to maximize their energy intake.

The study, by scientists at Oregon State University and the University of Hawaii, found that dolphins engage in a highly choreographed night-time “dance” to enclose their prey, and then dart into the circle of confused fish in organized pairs to feed for about 15 seconds, before backing out and letting the next pairs in line take their turn.

Results of the study were published this week in the journal, *Acoustical Society of America*.

“Synchronized swimmers have nothing on spinner dolphins,” said Kelly Benoit-Bird, a marine ecologist at Oregon State University and lead author on the study. “The degree of synchrony they display when feeding is incredible – especially considering that they’re doing it at night, several meters below the surface where they



[Slide Show](#)

[Nature's Born Phlebotomists](#)

can't see their prey or each other." The study is important, scientists say, because it greatly expands knowledge of spinner dolphin behavior and it opens up new fields of scientific inquiry into underwater ecosystems made possible by technological advancements in acoustical monitoring. It was funded by the National Science Foundation and the Office of Naval Research.

Much of the knowledge about spinner dolphin feeding has been anecdotal because they are primarily nocturnal in their feeding, Benoit-Bird pointed out. However, acoustical eavesdropping allowed the scientists to "view" the dolphins' behavior without interrupting their routine with lights and underwater cameras. In their study off the coast of Oahu, Hawaii, the scientists used sonar readings from a "multi-beam echo-sounder" to monitor groups of spinner dolphins. The animals' systematic approach to feeding was eye-opening.

Initially a small group of about 20 dolphins would swim side-by-side in a straight line until finding concentrations of prey – in this case, lanternfish. When they got to within five meters of their prey, they would pull into a tight circular formation and sequentially swim up and down vertically, in essence, doing "the wave" like fans at a sporting event, Benoit-Bird said.

"They were using their bodies like a plow," she said. "We're not sure if they were creating a pressure barrier or trying to confuse the prey. But the result among the lanternfish was chaos."

As the lanternfish became concentrated, the dolphins tightened their circle and formed 10 pairs. The pairs at one o'clock and seven o'clock would move in, feed for 15 seconds, and retreat back to the circle. Then the pairs at two o'clock and eight o'clock would do likewise. The feeding would last for about five minutes, during which time each dolphin got two opportunities to feed, and then the group rose as one to the surface to breathe, maintaining their circle. The dolphins would take one breath, Benoit-Bird said, and then dive down and begin the process anew.

"If one or two individual dolphins would break the circle or head to the surface to breathe, it breaks their whole system up," Benoit-Bird said. "They never did. So then you have to ask: How do they communicate with each other, and how do they pass on that knowledge to their young?"

The researchers are still working on the latter puzzle, but their acoustical monitoring study found that much of what scientists had assumed about dolphin communication may, in fact, be wrong in this species. In a companion article also published in *Acoustical Society of America*, the researchers describe how they used underwater hydrophones to listen to the dolphins during their feeding forays.

Dolphins are often vocal and their use of frequency-modulated whistles was thought by many to cue their coordinated behavior. But the researchers found they didn't use those whistles at all while hunting prey – just during non-foraging times or when they were surfacing. Instead, they used a series of "clicks," with the highest click rates taking place just prior to foraging.

"Whistles are omni-directional, like turning on a light bulb in a room," Benoit-Bird said. "Clicks, on the other hand, are directional like a laser. We think it may be a strategy to communicate only within the group and not to other potential lanternfish predators. Tuna and billfish are looking for the same prey and they can hear the whistles but not the clicks because the frequencies are too high and so focused.

"If you're lined up to eat this great smorgasbord, would you want to tell the tuna next door about it?"

Benoit-Bird's co-principal investigator on both papers was Whitlow W.L. Au, from the University of Hawaii.

Spinner dolphins are found primarily in tropical and subtropical waters, offshore and near island chains. They grow to a length of about six to seven feet, and feed on small, deep-ocean prey including lanternfish, shrimp and juvenile squid.

During their hunting forays, these athletic, acrobatic dolphins catch and consume a single fish at a time and each lanternfish may only be 3-5 inches long. To match their 3,200-calorie-per-day diet, they need to eat at least 650 fish each night – plus enough extra to fuel the energy they burn during the hunt, perhaps another 200 to 300 fish.

"To make that work, they need to eat about a fish a minute," Benoit-Bird said, "and we think that's why they've developed this elaborately complex system of group predation. Dolphins can't open their mouths like baleen whales and swallow large amounts of food at once. They have to target individual fish and it's too difficult and energy-consuming to hunt solo." "It's tough to make a living in the subtropical ocean, which is something of a biological desert," she added. "They've had to adapt these unique behavioral methods to maximize their ability to capture prey."

*Note to Editors: Animation of actual data from the dolphins hunting their prey is available below:*

[\*This top view of actual data from multi-beam sonar observations of dolphin foraging is shown at eight times real speed. The yellow dots show the position of each dolphin in this group of 20, while the purple background shows their prey. Each time the color purple becomes brighter, it represents a doubling in the numerical intensity of prey. This foraging occurs in four distinct phases, highlighting in the timeline at the top of the clip: 1\) Wide line, where the dolphins find a good spot in the prey to begin;\*](#)

2) Tight line, when the dolphins begin to herd the prey forward; 3) Circling, the separation of the herded prey from the rest of the prey; and 4) Inside circle, when dolphins move into the circle of food in pairs to eat

[This is a side view of data, also at 8X real speed.](#) The blue dots show dolphins behind the center of the circle of prey, while the yellow dots are dolphins in front of the plane. The brightness of the color purple increases with the density of prey and the four distinct foraging stages (see above) are visible. From this observation, it is apparent how the dolphins cover nearly the entire extent of the prey layer, working together to force it into a dense patch – first in front of the line of dolphins, and then within the circle of dolphins

[This visualization shows a 3-D representation of multibeam sonar data of foraging dolphins.](#) It becomes clear from this view how the dolphins work together to surround an entire slab of the layer of prey. They circle their prey, forming a cylinder of dense fish between them, before rising as one to breathe at the surface.

### Study documents safety problems for biological products

Approximately one in four biological medicinal products (such as antibodies, enzymes and insulin) approved since 1995 in the U.S. and Europe have had at least one safety-related regulatory action issued for them 10 years after their approval, including about 11 percent receiving a "black box" warning, according to a study in the October 22/29 issue of JAMA, a theme issue on the Health of the Nation.

Biologicals are preparations in which the active substance is produced by or extracted from a biological source, such as antibodies, enzymes and hormones. They represent an important and growing part of medical therapies, with more than 250 biologicals having been approved since 1982, according to background information in the article. "Between 2003 and 2006, biologicals represented 24 percent and 22 percent of all new chemical entities approved by the U.S. and EU [European Union] regulatory authorities, respectively," the authors write. "Biologicals are a relatively new class of medicines that carry specific risks (e.g., immunogenicity [the ability to stimulate an immune response]). However, limited information is available on the nature and timing of safety problems with their use that were identified after approval."

Thijs J. Giezen, Pharm.D., of Utrecht University, Utrecht, the Netherlands, and colleagues examined the nature and probability of safety-related regulatory actions issued for biologicals approved in the United States and/or the European Union between January 1995 and June 2007. Vaccines, allergenic products (a substance capable of causing an allergic reaction), and products for further manufacture and transfusion purposes were excluded.

A total of 174 biological medicinal products obtained approval during the study period, including 136 biologicals approved in the U.S. and 105 in the European Union, of which 67 biologicals obtained approval in both regions during this time. The researchers found that between January 1995 and June 2008, 82 safety-related regulatory actions were issued for 41 of the 174 biologicals (23.6 percent). These included 46 written communications (warnings of health hazards) to health care professionals in the U.S., 17 in the European Union, and 19 black box warnings (warning of serious health hazards). No biologicals were withdrawn due to safety reasons.

The average time to a safety-related regulatory action was 3.7 years and 70.7 percent of the safety-related regulatory actions were issued within five years after approval. The probability of a biological requiring its first safety-related regulatory action was 14 percent three years after approval and 29 percent ten years after approval. Biologicals that were the first to be approved in their chemical, pharmacological, and therapeutic subgroup had a significantly higher risk for the occurrence of its first safety-related regulatory action compared with later approved products.

The safety-related regulatory actions issued for biologicals mostly involved the system organ classes of general disorders and administration site conditions (26.8 percent of 82), infections and infestations (22 percent), immune system disorders (15.9 percent), and neoplasms benign, malignant, and unspecified (12.2 percent). "The safety-related regulatory actions issued in the system organ class of general disorders and administration site conditions can be partly explained by the infusion reactions occurring after the parenteral [intravenously or by injection] route of administration, which is the mode of administration for most biologicals. A more in-depth evaluation of the mode of action of biologicals might have predicted some safety problems during the developmental phase."

"Although the limitations of preclinical trials for biologicals are acknowledged, results from pharmacology studies, preclinical studies, and clinical studies might result in the prediction of potential risks related to the drug for which close monitoring is needed in the postapproval setting. Health care professionals should be aware of the specific risks related to the relatively new class of biologicals to be able to provide a link between the use of the biological and the patient presenting with a clinical problem," the authors write.

(JAMA. 2008;300[16]:1887-1896. Available pre-embargo to the media at [www.jamamedia.org](http://www.jamamedia.org))

**Editor's Note:** Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

### **Editorial: Prescription Drugs, Products Liability, and Preemption of Tort Litigation**

*In an accompanying editorial, Catherine D. DeAngelis, M.D., M.P.H., Editor-in-Chief, JAMA, and Phil B. Fontanarosa, M.D., M.B.A., Executive Deputy Editor, JAMA, Chicago, write that these findings show the need for improvement in the drug approval process and the postmarketing surveillance system.*

*"As shown in the study by Giezen et al, many safety problems are identified only after drug approval. The human body is in a constant state of change and the effects of some drugs will manifest only after exposure over time. Furthermore, some serious adverse drug effects are quite uncommon and require use of the drug in large numbers of patients to become evident. The safety of drugs in a clinical trial, the study type used for Food and Drug Administration approval, is based on specific participant types, numbers, and design that cannot ensure the true safety of a drug. In addition, manipulation of study results by the drug manufacturers (who almost always sponsor studies used for decisions about drug approval) can obscure the true safety profile of a drug."*

*"Given the current imperfect process for approval and the flawed postmarketing surveillance system, the drug and device regulation process is at best an inexact and incomplete science. Until these deficiencies in the system are remedied, some patients inevitably will continue to experience harm from the use of newly marketed products as well as from use of other approved medications. Just as with other consumer products that cause harms, consumers (i.e., patients) who are injured by defective medical devices or by pharmaceutical products with inadequate warnings of potential harms may have to resort to legal action as recourse for their injuries."(JAMA. 2008;300[16]:1939-1941. Available pre-embargo to the media at [www.jamamedia.org](http://www.jamamedia.org))*

### **Eating quickly and until full trebles the risk of being overweight**

#### ***The joint impact of self-reported behaviours of eating quickly and eating until full on overweight: results of a cross sectional survey***

The combination of eating quickly and eating until full trebles the risk of being overweight, according to a study published today on [bmj.com](http://bmj.com).

Until the last decade or so most adults did not have the opportunity to consume enough energy to enable fat to be stored. However, with the increased availability of inexpensive food in larger portions, fast food, and fewer families eating together and eating while distracted (e.g. while watching TV), eating behaviours are changing, and this may be contributing to the obesity epidemic.

Professor Iso and colleagues recruited over three thousand Japanese men (1,122) and women (2,165) aged 30-69 between 2003 and 2006 to examine whether eating until full and speed of eating are associated with being overweight. Participants were sent a diet history questionnaire about their eating habits including questions about eating until full and their speed of eating.

The researchers report that around half (50.9%) of the men and just over half (58.4%) of the women said they ate until they were full. And just under half (45.6%) of men and 36% of women said they ate quickly.

The group of participants who said they ate "until full and ate quickly" had a higher body mass index (BMI) and total energy intake than those who did not "eat until full and did not eat quickly". The researchers also found that both men and women in the "eating until full and eating quickly" were three times more likely to be overweight than the participants from the "not eating until full and not eating quickly" group.

The authors conclude that a combination of eating until full and eating quickly has "a supra-additive effect on overweight".

These findings demonstrate how current eating patterns may contribute to the current epidemic of obesity, say Elizabeth Denney-Wilson from University of NSW and Karen Campbell from Deakin University in Australia, in an accompanying editorial. They call on doctors to work with parents to encourage healthy eating habits in their children like eating slowly, serving appropriate portion sizes, and eating as a family in a non-distracting environment.

### **Erectile dysfunction gives early warning of a heart attack, warns expert**

#### ***Erectile dysfunction is best predictor of cardiovascular risk in men***

Erectile dysfunction gives a two to three year early warning of a heart attack, warns an expert on [bmj.com](http://bmj.com) today. But the link between erectile dysfunction and the risk of heart disease is being ignored by doctors, writes Dr Geoffrey Hackett from the Good Hope Hospital in Birmingham.

Over many years Hackett reports regularly seeing patients referred with erectile dysfunction after a heart attack, only to hear that they had developed erectile dysfunction two to three years before—a warning sign ignored by their general practitioners.

It is well known that erectile dysfunction (a symptom of vascular disease in the smaller arteries) doubles the risk of heart disease, a risk equivalent to being a moderate smoker or having an immediate family history of heart disease. Erectile dysfunction in type 2 diabetes has been shown to be a better predictor of the risk of heart disease than high blood pressure or high cholesterol.

But despite this considerable evidence erectile dysfunction is still treated as a recreational or "lifestyle issue" rather than a predictor of a serious health problem, says Hackett.

The UK government has pledged to reduce the death rate from coronary heart disease and stroke and related diseases in people under 75 by at least 40% by 2010, yet there is no screening for erectile dysfunction in patients with diabetes or heart disease, he says.

"Continuing to ignore these issues on the basis that cardiologists feel uncomfortable mentioning the word 'erection' to their patients or that they may have to deal with the management of a positive response, is no longer acceptable and possibly, based on current evidence, clinically negligent", he concludes.

### **RSV may hide in the lungs, lead to asthma, UT Southwestern researchers report**

DALLAS – Oct. 21, 2008 – Conventional wisdom has been that respiratory syncytial virus (RSV) – a common virus that causes infection in the lungs – comes and goes in children without any long lasting impact.

A study conducted in mice by UT Southwestern Medical Center researchers, however, suggests that RSV may hide in the lungs even after other symptoms abate, ultimately resurfacing to cause recurrent wheezing and chronic airway disease.

"This research suggests that there's a potential new mechanism for asthma related to viral infections in children that could be associated with RSV," said Dr. Asuncion Mejias, assistant professor of pediatrics at UT Southwestern and senior author of a study available online and in the Nov. 15 issue of the *Journal of Infectious Diseases*. "These findings could aid in the development of preventive and therapeutic interventions for children with recurrent wheezing due to a virus such as RSV."

RSV is the leading cause of viral respiratory infections and hospitalizations in infants and children worldwide. Half of all babies develop an RSV infection within the first year of life and practically all have had at least one RSV infection by age 3, said Dr. Octavio Ramilo, professor of pediatrics at UT Southwestern and study co-author. About 3 percent to 10 percent of infants with RSV infections develop severe bronchitis and require hospitalization. Most children recover within a week, but RSV can cause repeated infections throughout life. There is currently no vaccine available.

Dr. Ramilo said the team's findings contradict the current thinking that ribonucleic acid viruses like RSV are easily destroyed. "Whether RSV persists in children remains to be seen, but the fact that the virus persists in mice is amazingly powerful," he said.

The most striking finding, Dr. Mejias said, is that the amount of virus detected in the lungs of the mice directly correlates with the severity of airway hyperreactivity. Airway hyperreactivity, or episodes of bronchospasms in humans, is the main characteristic of asthma.

Doctors at UT Southwestern have previously shown that RSV infection could increase the risk of developing asthma. In 2004, researchers including Drs. Mejias and Ramilo monitored mice infected with RSV and found that infected mice were more likely to develop chronic lung disease than healthy mice. They also found that infected mice treated with an anti-RSV antibody had less virus in the lungs and not only showed improvement during the acute disease, but also developed significantly less airway hyperreactivity and lung inflammation during the chronic phase of the disease.

"If you use an antibody against RSV, you not only prevent acute disease from the infection but you can also prevent the development of the asthma phenotype, indicating that early interventions against the virus can have a long-term benefit," Dr. Mejias said.

To determine whether RSV persisted in the lungs, UT Southwestern researchers infected mice with live RSV, ultraviolet-light-treated RSV or heat-inactivated RSV. They then monitored the mice for 42 days, checking their pulmonary function and respiratory rate at set intervals. At the end of the study, the researchers found evidence of the virus in every mouse infected with live RSV, but not in the other groups.

While studies of adults with chronic obstructive pulmonary disease have suggested that RSV may persist, this is the first study to test the hypothesis in this animal model of RSV-induced asthma. The persistence of the virus in children has not been extensively researched, Dr. Ramilo said.

Dr. Mejias said the next step is to determine whether RSV persists in children.

"We are currently doing a study in which we are treating kids with a new antibody that is very potent," she said.

"The plan is to follow them for a year to see if aggressive treatment against the virus can prevent wheezing."

*Other UT Southwestern researchers involved in the study were Dr. Juan Pablo Torres, visiting senior researcher in pediatrics; Drs. Cynthia Somers and Steve Grube, fellows in pediatric infectious disease; Drs. Dora Estripeaut and Claudia Tagliabue, former postdoctoral fellows in pediatric infectious disease; Shama Khokhar and Aneta Wozniakowski, research assistants in pediatrics; Vijay Bhoj, graduate student in immunology; Dr. Ana Gomez, assistant professor of pathology; and Dr. Hasan Jafri, former assistant professor of pediatrics.*



## **Chronic inflammation can help nurture skin cancer, study shows**

**Toni Baker** - 2008 October 21

Inflammation, a frontline defense against infection or disease, can help nurture skin cancer, researchers have found. IDO, an enzyme that works like a firefighter to keep inflammation under control, can be commandeered to protect early malignant cells, say Medical College of Georgia researchers studying an animal model of chronic inflammation and skin cancer.

"Inflammation should really help prevent a tumor," says Dr. Andrew Mellor, director of the MCG Immunotherapy Center and Georgia Research Alliance Eminent Scholar in Molecular Immunogenetics. In fact, there is strong evidence that inflammation triggers the immune response. "You want a good immune response; this is what protects you from pathogens," he says. "In this case, it's an unfortunate exploitation by malignant cells."

In a study with Drs. George C. Prendergast and Alexander J. Muller at the Lankenau Institute of Medical Research in Philadelphia, researchers gave mice a single dose of a carcinogen at the same time they began painting a tiny portion of skin with a poison ivy derivative twice weekly for 20 weeks.

IDO quickly became part of the mix, creating a "suppressive" immune response that helped resulting precancerous cells grow into tumors, according to research published online in Proceedings of the National Academy of Sciences. When they used the same protocol in a mouse in which IDO had been genetically deleted, tumor development dropped off dramatically.

The scenario is analogous to chronic sun exposure and skin cancer, says Dr. Mellor, the study's corresponding author. Ultraviolet radiation in sunlight causes malignant skin cells to appear but sun exposure also causes skin inflammation - evidenced by sunburn. The significance of the new study is that the researchers have shown that IDO, or indoleamine 2,3-dioxygenase, may be produced as a part of the inflammatory mix, which could then protect the malignant skin cells. "'Chronic' is the key word," Dr. Mellor says, noting high melanoma rates in Australians, for example, who live deep in the southern hemisphere.

"We have long suspected that IDO is a component of certain kinds of inflammation that create suppression," says Dr. Mellor. IDO's "firefighter" role probably resulted from the body's need to control inflammation in areas such as the gastrointestinal tract. The GI tract is constantly bombarded by food and microbes which could lead to debilitating and deadly inflammation.

"You really set a fire," Dr. Mellor says of inflammation. In fact, the English word inflammation comes from the Latin word inflamatio, which means to set a fire. But instead of helping protect healthy tissue as it does in the GI tract, IDO becomes problematic in cancer.

The latest finding shows IDO has a more important and earlier role than we thought in tumor formation, says Dr. Mellor. He and colleague Dr. David Munn led a research team that 10 years ago showed fetuses use IDO to avoid rejection by the mother's immune system. They and others have subsequently shown that tumors, including melanoma, as well as infectious agents such as HIV also use IDO to escape an immune attack. "IDO favors the tumor: The immune system basically sits back and watches the tumor grow," says Dr. Mellor.

Transplant patients, who require generalized immune inhibitors to keep their transplanted organs, also can be victims of this suppressive inflammation, says Dr. Mellor, noting their high risk of lymphoma after a few years of therapy.

The IDO inhibitor they have been using for years in the lab is now under study in breast cancer patients receiving chemotherapy. Drs. Mellor and Munn also have recruited Dr. Yukai He, cancer vaccine researcher, to MCG to work with them on how vaccines designed to direct an immune attack can work synergistically with the IDO inhibitor.

## **UCSB researchers develop cross-protective vaccine**

Santa Barbara, Calif. - Doctors have always hoped that scientists might one day create a vaccination that would treat a broad spectrum of maladies. They could only imagine that there might be one vaccine that would protect against, say, 2,500 strains of Salmonella. And what if that same vaccine could help protect the elderly?

UCSB scientists Douglas Heithoff and Michael Mahan — along with University of Utah scientists Elena Enioutina, Diana Bareyan, and Raymond Daynes — believe their recent research suggests that might be possible in the not-too-distant future. In a paper to be published in the November edition of the journal Infection and Immunity, the researchers detail the path to creating a vaccine that confers protection against multiple strains of bacteria.

"Vaccines are great," Mahan said in an interview. "Second to water sanitation, they are the best medical invention of mankind." The problem with conventional vaccines is that they only protect against a limited number of closely related strains. "That is why flu vaccines need to be administered every year because

different flu strains arise every year," Mahan said. This is what prompted the researchers to begin their quest for a more powerful vaccine that conferred protection against many strains.

The team focused on developing a vaccine against Salmonella, which causes food and blood poisoning — with over 1.5 million cases in the United States each year. "It's endemic worldwide," Mahan said. "It's not a carnivore issue — it's everybody's issue since fruits and vegetables are often the source of infection."

By disarming a "genetic switch," the research team has developed a vaccine that protects against many strains of Salmonella. The new vaccine stimulates the production of antibodies and immune cells that work together to kill bacteria. Also, the vaccine does not induce a specific class of inhibitory immune cells that are known to contribute to immune declines in cancer patients. This lack of "immune suppression" is an advantage of the new vaccine over conventional vaccines.

The researchers also showed a link between the immune declines observed in cancer patients and those occurring as part of the normal aging process. "This may explain why the elderly are more susceptible to infection and why they are more difficult to effectively vaccinate," Mahan said. "Protocols that remove these inhibitory cells may boost vaccine effectiveness in the elderly."

The impact on human health may come in the near term. The new vaccine is currently being tested in livestock — the main source of human infection. "The immunization of livestock can help human health by promoting food safety," Heithoff said. "Of course, the three principal issues for vaccines will always be safety-safety-safety — and we've put a lot of effort into it."

*Funding for this research came from the National Institutes of Health, the United States Department of Agriculture, and the Mathers Research Foundation.*

## **From a Strip of Scotch Tape, X-Rays**

**By KENNETH CHANG**

In a tour de force of office supply physics, researchers at the University of California, Los Angeles, have shown that it is possible to produce X-rays by simply unrolling Scotch tape.

Next step: nuclear fusion.

"We're going to do that," said Seth J. Putterman, a professor of physics at U.C.L.A. "I think it will work."

But first, X-rays.

In the current issue of the journal *Nature*, Dr. Putterman and his colleagues report that surprisingly fierce flows of electrons were unleashed as the tape was unpeeled and its gooey adhesive snapped free of the surface. The electrical currents, in turn, generated strong, short bursts of X-rays — each burst, about a billionth of a second long, contained about 300,000 X-ray photons.

"Some kind of microscopic lightning effect," Dr. Putterman said.

The scientists even demonstrated that the X-rays were bright enough to take an X-ray of a finger.

That does not mean that tape dispensers on office desks are mini X-ray machines. So far, the phenomenon has been observed only when the tape is unpeeled in a vacuum. Something about air — perhaps moisture — short-circuits the X-rays.

The work is not unprecedented. In 1939, scientists demonstrated that peeling tape emits visible light — an easy experiment anyone can conduct in a closet. But visible light photons have only about one-10,000th the energy of an X-ray photon.

Russian scientists reported as far back as 1953 that they had detected X-rays from tape. "But as far as I can tell, no one ever believed them," Dr. Putterman said. "It was a big surprise to discover this deep dark corner of past research."

All of the experiments were conducted with Scotch tape, manufactured by 3M. The details of what is occurring on the molecular scale to generate high-energy photons are not known, the scientists said, in part because the Scotch tape adhesive remains a trade secret.

Other brands of clear adhesive tapes also gave off X-rays, but with a different spectrum of energies. Duct tape did not produce any X-rays, Dr. Putterman said. The scientists have not yet tested masking tape.

The research opens up the possibility of looking for similar X-ray emissions from composite materials as they fatigue. Such materials, increasingly used in airplanes and automobiles, are stronger and lighter than many metals, but they do not show the visible weaknesses that metals do before breaking.

The tape phenomenon could also lead to simple medical devices using bursts of electrons to destroy tumors. The scientists are looking to patent their ideas.

And finally, there's the possibility of nuclear fusion. If the energy from the breaking adhesive could be directed away from the electrons to heavy hydrogen ions implanted in modified tape, the ions would accelerate fast enough so that when they collided, they could fuse together and give off energy — the same process that lights the sun.

## Assessing the quality of phase I clinical trial abstracts

Geneva, Switzerland: Researchers have developed a method of assessing the quality of phase I clinical trial abstracts submitted to two different oncology conferences: EORTC-NCI-AACR (ENA) [1] and American Society of Clinical Oncology (ASCO). The results, presented on Thursday (23 October) at the 20th ENA Symposium on Molecular Targets and Cancer Therapeutics in Geneva, show there is room for improvement and the researchers suggest authors of conference abstracts should adopt guidelines for reporting phase I clinical trials.

Dr Jeremy Ho, an internal medicine resident under the supervision of associate professor Dr Lillian Siu at the Princess Margaret Hospital (Toronto, Canada), had worked with colleagues to develop a quality score for abstracts based on an electronic survey of experts. They had used it to measure the quality of 1,683 phase I abstracts published in the ASCO Annual Proceedings from 1997 to 2006, and then they used the same method to measure the quality of 304 abstracts presented at the ENA symposia from 2003-2007.

When they compared abstracts on phase I trials from the period where there was an overlap between the two conferences (2003-2006), they found that the mean average quality score for the 229 ENA abstracts was 69.6% compared to 64.5% for the 713 ASCO abstracts.

Dr Ho said: "ASCO is a much bigger meeting than ENA, with different objectives, scope and audience. Our study is not meant to be a direct comparison to criticise the quality of abstracts submitted to either meeting. The data enable us to gain insight on areas where improvements in the quality of phase I trial abstract reporting can be made, regardless of the meeting.

"The slightly higher quality score for the ENA abstracts is probably due to a higher figure for the maximum number of characters allowed per abstract (2,500 for ENA and 2,000 for ASCO), an allowance for updating previously presented data, and the more specialised anti-cancer drug development focus of the ENA symposia. There remains room for improvement in both conferences for improving abstract quality and we believe this may be achieved by adopting guidelines for reporting on phase I clinical trials."

Dr Ho and his colleagues have drawn up a list of what they believe should be included in any guidelines on reporting phase I trials.

### **The following are items that are absolutely essential:**

- \* Description of dose-limiting toxicity encountered on study
- \* Conclusion explicitly states maximum tolerated doses (MTD) or residual disease (RD) or reason for early trial closure
- \* Description of grade three toxicity and above that may be related to study drug
- \* Description of drug delivery schedule or formulation
- \* Number of patients on study
- \* Title identifying study as dose finding or phase I
- \* Pharmacokinetic analysis, if applicable

### **The following items should also be reported:**

- \* Explicit definition of primary end point or objective
- \* Rationale for study
- \* Pharmacodynamic results, if applicable
- \* Current status of study
- \* Information related to treatment cycles
- \* Efficacy outcome of patients
- \* Number of patients at each dose level
- \* Tumour types of responders, if applicable

Dr Ho said: "We are not aware of any such guidelines in existence. We are hoping that our suggestions for guidelines can be validated further and then put into clinical use, for instance, as recommendations and reference guide to clinical researchers to help them with abstract writing, and maybe also as guidelines for conferences to evaluate abstracts being submitted."

Abstracts at both conferences improved in quality the more recently they were presented, possibly indicating that authors were becoming more aware of what information needed to be included.

Dr Ho said he and his colleagues concentrated on phase I clinical trials for a number of reasons. "Phase I trials are unique in that they evaluate new drugs or drug combinations, and provide necessary foundations for the development of safe and more effective anti-cancer therapies. These trials are often initially presented in abstract format at major cancer conferences. Results of phase I trials published in abstract format frequently influence further research endeavours in higher-phase trials before full peer-reviewed publication occurs.

"We hope that this study will help to raise awareness about the importance of improving abstract quality in oncology conferences and in the cancer literature." *Abstract no: 382.*

*Notes:[1] EORTC [European Organisation for Research and Treatment of Cancer, NCI [National Cancer Institute], AACR [American Association for Cancer Research].*

### **X marks the spot: Sharpies get thumbs-up for marking surgery sites**

A bit of good news out of the Faculty of Medicine & Dentistry at the University of Alberta for patients undergoing surgery or an invasive procedure, their surgeons and cost-conscious hospital administrators. It's standard practice for the surgeon or their designate, (in consultation with the patient when possible), to mark the operative/invasive site using a marking pen before an operation, a precaution to ensure surgeons cut the correct spot. But there was concern that germs would be spread from one patient to the next, so it has also become common procedure to throw away the marker each time, costing thousands of dollars a year.

Turns out hospital staff were putting too fine a point on it, say a couple of infection control specialists at the U of A who looked into the matter. Associate professor Dr. Sarah Forgie of the Department of Pediatrics and pediatric infectious diseases resident Dr. Catherine Burton have shown that the tips of the Sharpies® don't spread infection since the ink has an alcohol base.

This has caught the attention of organizers of a major conference on infectious disease taking place in Washington, D.C., at the end of October. They have invited Burton to share her work with other disease control specialists from around the world, an honour for the resident.

After asking around and finding out that many of the surgical teams in Edmonton liked using Sharpie® brand markers, Forgie and Burton decided to put the common, everyday brand to the test along with another brand, the second one a sterile marker specifically intended for single use in operating rooms.

In a controlled experiment, marker tips were heavily contaminated with four types of bacteria that can cause surgical site infections; two of the germ types are of particular concern in hospitals since they are antibiotic-resistant, Burton explained.

After recapping the markers and letting them sit for 24 hours, Burton and Forgie found that the sterile, one-use marker, which has a non-alcohol-base ink, was still contaminated. But the Sharpies® were not.

In collecting an extremely large number of germs on the markers during their experiment, "we went much further than what would happen in real life," said Forgie.

She is confident that the marking tip of Sharpies® does not pose a risk of bacterial transmission. As long as the rest of the pen is cleaned with an alcohol swab between patients (just as is done with stethoscopes), the Sharpies® do not need to be discarded after each use. Safety is the priority, and in this case it can be done economically, Forgie said.

### **Magnetic brain therapy gets US green light**

\* 11:45 21 October 2008

\* NewScientist.com news service

\* **Linda Geddes**

It has been touted as a possible treatment for migraine, depression, and stroke, and is even said to have roused a patient from a coma. Now transcranial magnetic stimulation (TMS) has received its first stamp of approval as a therapy by the US Food and Drugs Administration, which says TMS can be used to treat depression in adults who don't respond to anti-depressant drugs.

TMS involves holding an electromagnetic coil over the head and using it to stimulate the underlying brain tissue. Rapidly changing magnetic fields induce weak electric currents in brain tissue, either exciting or inhibiting brain cells, and making it easier or harder for them to communicate with one another.

Several large trials have suggested TMS can be useful in treating depression, where it is used to excite cells in the areas of the brain involved in mood regulation.

In the latest trial, submitted to the FDA by Neuronetics of Malvern, Pennsylvania, which develops TMS devices, more than half of depressed patients showed an improvement in symptoms after receiving five 40-minute TMS sessions per week for four to six weeks.

#### **Remaining doubts**

"I am delighted that patients with depression have a new treatment option without the side effects of medications," says Mark George of the Medical University of South Carolina, Charleston, who pioneered the use of TMS in depression during the mid 1990s.

However, he cautions that some scientists remain sceptical about the effectiveness of TMS, because participants in clinical trials can usually tell if they are getting a sham treatment or not. George is currently conducting a trial which may solve the issue, as the sham treatment feels more similar to the real thing. "We will have what I hope will be the definitive statement about whether TMS really works," he says. The results are expected next year.

Others welcomed the FDA approval, but added that further studies were needed to establish the optimum dose, and which patients are most likely to benefit.

"Only some patients respond to TMS for depression, so part of the process for optimising it is to find ways of screening patients," says Vincent Walsh of University College London.

The FDA's approval may also open the floodgates for medical devices companies hoping to get TMS approved in other countries. "It is a very significant step forward," says Andrew Thomas of UK-based TMS company Magstim.

### **Job choice 'affects Alzheimer's'**

#### ***Going to university, then choosing a mentally demanding job may help protect the brain from the devastating impact of Alzheimer's disease on memory.***

Scientists found tissue damage was much quicker to lead to memory loss in the less intellectually stimulated.

They suggest mentally tough work, or genes which help people achieve such careers, may help the brain compensate for disease. The Italian research was published in the journal *Neurology*.

While there are a number of studies which, based on age and symptoms, suggest that mental stimulation can ward off Alzheimer's, there are fewer which look directly at the damage wreaked by the illness on the brain.

The team from the San Raffaele University in Milan used brain scanners to look for the distinctive "tangles" and protein deposits characteristic of Alzheimer's in 242 older people, 72 who had mild cognitive impairment, and 144 with no memory problems.

Over a 14-month period, 21 of the people with mild impairment went on to be diagnosed with Alzheimer's. However, when the MRI scans of people with the same level of memory problems were compared, the damage was significantly more extensive in those who had been university educated, then progressed to mentally-tough careers.

According to the researchers, this meant that, somehow, the brain was managing to cope better with the disease, perhaps by creating a "cognitive reserve" which buffered against its effects.

#### **Brain training**

Dr Valentina Garibotta, who led the research, said: "The brains are able to compensate for the damage and allow them to maintain functioning in spite of damage. "There are two possible explanations - the brain could be made stronger through education and occupational challenges, or, genetic factors that enabled people to achieve higher education and occupational achievement might determine the amount of brain reserve."

A spokesman for the Alzheimer's Society said that more research was "urgently needed" to build on the findings, and perhaps find ways to help people manage their symptoms. "This research is exciting as it is the first study to use MRI scanning extensively to show that in early Alzheimer's, people with higher education have fewer symptoms of dementia than others with the same level of damage to the brain. "Previously, research has suggested that people with "cognitive reserve" do better at managing the symptoms of dementia, but until now there has been little physical evidence."

### **Scientists unlock secret of death protein's activation**

#### ***May lead to drugs that force cancer cells to self-destruct***

BOSTON--Scientists at Dana-Farber Cancer Institute have identified a previously undetected trigger point on a naturally occurring "death protein" that helps the body get rid of unwanted or diseased cells. They say it may be possible to exploit the newly found trigger as a target for designer drugs that would treat cancer by forcing malignant cells to commit suicide.

Loren Walensky, MD, PhD, pediatric oncologist and chemical biologist at Dana-Farber and Children's Hospital Boston, and colleagues report in the Oct. 23 issue of the journal *Nature* that they directly activated this trigger on the "executioner" protein BAX, killing laboratory cells by setting in motion their self-destruct mechanism.

The researchers fashioned a peptide (a protein subunit) that precisely matched the shape of the newly found trigger site on the killer protein, which lies dormant in the cell's interior until activated by cellular stress. When the peptide docked into the binding site, BAX was spurred into assassin mode. The activated BAX proteins flocked to the cell's power plants, the mitochondria, where they poked holes in the mitochondria's membranes, killing the cells. This process is called apoptosis, or programmed cell death.

"We identified a switch that turns BAX on, and we believe this discovery can be used to develop drugs that turn on or turn off cell death in human disease by targeting BAX," said Walensky, who is also an assistant professor of pediatrics at Harvard Medical School.

BAX is one of about two dozen proteins known collectively as the BCL-2 family. The proteins interact in various combinations leading to either the survival of a cell or its programmed self-destruction. Cancer cells have an imbalance of BCL-2 family signals that drives them to survive instead of dying on command.

The late Stanley Korsmeyer, MD, an apoptosis research pioneer and Walensky's Dana-Farber mentor, had suggested that killer proteins like BAX could be activated directly by "death domains," termed BH3, contained within a subset of BCL-2 family proteins. He hypothesized that this activating interaction was a fleeting "hit-and-run" event, making it especially challenging for scientists to study the phenomenon.

As suspected, the proposed BAX-activating interactions could not be captured by traditional methods. "When you tried to measure binding of the BH3 subunits to BAX, you couldn't detect the interaction," explained Walensky. He recognized, however, that the BH3 peptides being used in the laboratory didn't retain the coiled shape of the natural BH3 domains that participate in BCL-2 family protein interactions. Walensky and his colleagues pioneered the design of "stapled" BH3 peptides, which contain a chemical crosslink that locks the peptides into their natural coiled shape. With biologically active shape restored, the stapled BH3 peptides bound directly to BAX and triggered its killer activity.

Defining how the activating peptides docked on BAX remained a formidable catch-22. In order to solve the structure of an interaction complex, it needed to be stable enough for analysis. In this case, the BH3 binding event itself triggers BAX to change its shape and self-associate to perform its killer function, rendering the activating interaction unstable by definition.

What if, Walensky proposed, you could set up the interaction of BH3 and BAX under laboratory conditions that caused it to be more stable or proceed in slow motion? The plan was to adjust the potency of the stapled BH3 peptide so that, according to Walensky, "it was good enough to bind BAX, yet activate it just a bit more slowly so that we could actually study the interaction." The researchers would then look for any detectable shift in the three-dimensional structure of the BAX protein to help point them to the docking site.

The researchers used nuclear magnetic resonance (NMR) spectroscopy to monitor the arrangement of atoms in the protein. First authors of the Nature paper Evripidis Gavathiotis, PhD, of Walensky's laboratory and Motoshi Suzuki, PhD, of Nico Tjandra, PhD's laboratory at the National Institutes of Health, succeeded in generating pure BAX protein that could be put into solution with the stapled BH3 peptide -- the latter in increasing concentrations until it initiated a BH3-BAX interaction. Gavathiotis and Suzuki used the NMR technique to spot a group of BAX amino acids, the building blocks of proteins, which were affected by the addition of the stapled BH3 peptide.

"The discrete subset of amino acids that shifted upon exposure to the stapled BH3 peptide mapped to a completely unanticipated location on BAX," said Walensky. The long-elusive binding site on BAX that initiates its killer activity was revealed. "Because BAX lies at the crossroads of the cell's decision to live or die, drugs that directly activate BAX could kill diseased cells like in cancer and BAX-blocking drugs could potentially prevent unwanted cell death, such as in heart attack, stroke, and neurodegeneration," said Walensky. *Additional authors include Marguerite Davis, Kenneth Pitter, Gregory Bird, PhD, and Samuel Katz, MD, PhD, of Dana-Farber, and Ho-Chou Tu, Hyungjin Kim, and Emily H.-Y. Cheng, MD, PhD, of Washington University School of Medicine, St. Louis.*

### **New study suggests that high-dose hormone treatment might reduce risk for PTSD**

Philadelphia, PA – Cortisol helps our bodies cope with stress, but what about its effects on the brain? A new study by Cohen and colleagues, appearing in the October 15th issue of Biological Psychiatry, suggests that the answer to this question is complex. In an animal model of posttraumatic stress disorder (PTSD), high doses of a cortisol-related substance, corticosterone, prevented negative consequences of stress exposure, including increased startle response and behavioral freezing when exposed to reminders of the stress. However, low-dose corticosterone potentiated these responses. This finding suggests that corticosterone levels may influence both vulnerability and resilience in a dose-dependent manner through its involvement in memory processes.

One of the complexities in understanding PTSD is the context-dependency of adaptation. In some situations, for example following a car accident in an otherwise secure community, one objective of treatment is to restore a sense of normalcy and control of one's life. Within this context, the high-dose corticosterone would seem to be the indicated treatment. However, one could imagine scenarios where hypervigilance and heightened emotional reactivity could be adaptive, perhaps in a combat zone. In that case, the lower and more typical corticosterone levels might help soldiers adapt to the continuing risks of combat. But, people do not spend their lives in a single context. "In the case of helping soldiers adjust to the stress of war, we have to think both short-term and long-term, to help soldiers adjust to combat, but also to help them return from combat to resume peacetime life. Thus, we need further guidance from animal research about how to help soldiers adjust flexibly across contexts, from the battlefield to the breakfast table," as explained by John H. Krystal, M.D., Editor of Biological Psychiatry and affiliated with both Yale University School of Medicine and the VA Connecticut Healthcare System.

Corresponding author Dr. Hagit Cohen concludes that, "single high-dose corticosteroid treatment may thus be worthy of clinical investigation as a possible avenue for early pharmacotherapeutic intervention in the acute phase, aimed at prevention of chronic stress-related disorders, such as PTSD. In this sense, it brings treatment of PTSD to a new era – an era of secondary prevention."

**Notes to Editors:**

*The article is "Early Post-Stressor Intervention with High-Dose Corticosterone Attenuates Posttraumatic Stress Response in an Animal Model of Posttraumatic Stress Disorder" by Hagit Cohen, Michael A. Matar, Dan Buskila, Zeev Kaplan, and Joseph Zohar. Authors Cohen, Matar, and Kaplan are affiliated with the Ministry of Health Mental Health Center, Anxiety and Stress Research Unit, and Buskila is from the Department of Medicine, Soroka Medical Center, all at the Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel. Zohar is affiliated with the Chaim Sheba Medical Center, Sackler Medical School, Tel-Aviv University, Israel. The article appears in Biological Psychiatry, Volume 64, Issue 8 (October 15, 2008), published by Elsevier.*

*The authors' disclosures of financial and conflicts of interests are available in the article. Dr. Krystal's disclosures of financial and conflicts of interests are available here.*

*Full text of the article mentioned above is available upon request. Contact Jayne M. Dawkins at (215) 239-3674 or ja.dawkins@elsevier.com to obtain a copy or to schedule an interview.*

### **Silencing a protein could kill T-Cells, reverse leukemia**

Blocking the signals from a protein that activates cells in the immune system could help kill cells that cause a rare form of blood cancer, according to physicists and oncologists who combined computer modeling and molecular biology in their discovery.

Researchers say the breakthrough could provide more efficient ways of targeting diseases such as leukemia, and help in the potential development of vaccines for viruses that cause AIDS.

The human immune system has a two-part strategy when dealing with infections. It generates antibodies that bind with bacteria and viruses to neutralize them. For a short time, the immune system also produces large numbers of a type of white blood cell, cytotoxic T-cell that kills other infected cells.

Once the pathogens are eliminated, these killer T-cells quickly die on their own, save for a few that remain in case the same infection returns. But in rare cases, these cells fail to follow their scripted lifecycle.

"When these cells don't normally die, they expand gradually over time and start attacking the body itself," said Thomas Loughran, M.D., lead author and director of Penn State Hershey Cancer Institute. "They can attack the joints to cause autoimmune diseases such as rheumatoid arthritis, and attack the bone marrow to cause leukemia."

Loughran, professor of medicine, and his Penn State colleagues are trying to tease out the conditions that cause the abnormal expansion of T-cells and trigger a disease known as large granular lymphocyte leukemia. So they constructed an intricate computer model illustrating the signaling network involved in the activation of the T-cells, as well as their programmed death.

The network model strings together complex data of molecular pathways inside a cell involving hundreds of genes and proteins and tries to predict an outcome based on how the genes and proteins interact.

"The interactions among proteins make them turn ON or OFF or intermittently ON or OFF to get billions of possibilities with hundreds of proteins," said Reka Albert, co-author and Penn State associate professor of physics and biology. "By simulating the protein interactions and tracing the ON/OFF states of all those proteins at the same time, we can see whether the cells live or die."

Albert explains that the model could help researchers zero in on the exact location of the signaling abnormalities that are keeping T-cells from dying. Once that is known, specific genes or proteins could be targeted with drugs to get rid of the abnormality.

Sifting through the billions of possibilities projected by the model, the researchers have found two proteins – IL-15 and PDGF – that appear to be crucial in keeping the T-cells alive. While IL-15 is key to the survival and activation of T-cells, PDGF stimulates the growth of those cells.

"You need the presence of both these proteins to create conditions in which the cytotoxic T-cells can proliferate," said Loughran, whose team's findings were recently published this week in the Proceedings of the National Academy of Sciences. "That is a major point of the discovery."

The researchers have also discovered another signaling protein -- NFκB -- controlled by the two proteins, which protects cancer cells from dying if it is over expressed.

"NFκB controls a host of other proteins related to inflammation in the body and our model suggests that if we keep it in the OFF state, it is able to induce cell death in the T-cells," explained Albert, who, together with graduate student Ranran Zhang, created the model. "In other words, we can reverse the disease by setting this molecule OFF."

When researchers blocked NFκB with drugs in cells from leukemia patients, they found a significant increase in mortality among the abnormal T-cells, suggesting that NFκB helps in the survival of leukemia cells.

"Basically when this protein is inhibited and not expressed anymore, the cells die," said Loughran. "It validates our model."

It is still unclear as to what prevents the T-cells from dying off, though researchers suspect that a chronic virus might be continually activating the cells. However, there is no clear evidence for the theory, but network modeling may be a start.

According to Albert, such models could save time and money in pointing out promising candidates – genes and proteins – for drug delivery. "Our model provides a shortlist of therapeutic targets that can be manipulated with drugs to kill off leukemia cells," she added.

The Penn State researchers are also looking to harness errant behavior of the T-cells in combating other deadly diseases. "In complicated infections like HIV, and in diseases such as cancer, you need to have an immune response that comprises both antibodies and cytotoxic T-cells," explained Loughran. "The problem is nobody has been able to generate a long-lived cytotoxic T-cell response in normal people." Since T-cells in people suffering from large granular lymphocyte leukemia are active, long-lived, and function like killer T-cells, Loughran believes that if his team can unlock the secret behind these cells' longevity, then T-cells in normal healthy people could be equipped with the same ability to fend off other deadly infections.

"The key is to find the master control switches that keep these cells alive," said Loughran, whose work is funded by the National Institutes of Health and the National Science Foundation. "And maybe those could be blocked directly."

*Other researchers on the paper include Ranran Zhang and Mithun V. Shah, both graduate students; Jun Yang, M.D., assistant professor; Susan B. Nyland, Ph. D., assistant professor of medicine; Xin Liu, Ph. D., assistant professor and Jong K. Yun, Ph. D., associate professor of pharmacology, all at Penn State Hershey Cancer Institute.*

### **Drug grenades explode right on target**

\* 13:25 22 October 2008

\* NewScientist.com news service

\* **Colin Barras**

Detonating explosives near sick people is not generally a good idea, but microscopic grenades that go off painlessly inside the body could accelerate the delivery of drugs to diseased tissue, say researchers.

Carbon nanotubes and other nanomaterials are touted as being perfect "mules" to deliver drugs because they can pass freely into cells and even cell nuclei. But the tiny structures diffuse very slowly through biological tissue, which could limit their therapeutic benefit.

[\*\*Download video! Nanoparticles packed with drugs can be delivered to tissue faster if they are loaded into larger exploding capsules \(Footage courtesy ACS\)\*\*](#)

Typically, 200-nanometre particles take nearly 9 hours to diffuse just 400 micrometers in water, says Bruno De Geest, a chemical engineer at Ghent University in Belgium.

But De Geest and colleagues can propel nanoparticles the same distance 800 times faster by hurling them from an exploding microscopic grenade.

#### **Sweet centre**

Their tiny grenades are made from a rigid but porous polymer membrane that contains a gel based on the sugar dextran. As water seeps through the membrane it degrades the chemical cross-links holding the gel together. The gel swells and eventually bursts the capsule open, spewing its contents outwards.

De Geest's team loaded the gel with green fluorescent nanoparticles to make it possible to see the explosive ejection (see video, top right). "To obtain exploding microcapsules that exhibit that behaviour, we need them to be between 100 and 400 micrometers [in diameter]," says De Geest.

#### **Smart bombs**

Smaller microgrenades can't be loaded with enough gel to cause a powerful detonation, he says. Although 400-micrometer-wide particles are too large to pass through the bloodstream – and so couldn't be injected into a vein – they could be implanted just below the skin in the area where the medicine is needed, says De Geest.

"For the purpose of vaccination, the subcutaneous region is an ideal place for antigen delivery," he says. He adds that the microcapsules are too small to cause any pain when they explode.

By altering the properties of membrane and payload it is possible to make the grenades in smaller sizes. The gel responds to temperature and pH too, so it would also be possible to build smart grenades targeted to a particular tissue environment. *Journal reference: Journal of the American Chemical Society (DOI: 10.1021/ja806574h)*





## Drugs Found in Hair of Ancient Andean Mummies

Charles Q. Choi for National Geographic News October 22, 2008

The first hard evidence of psychoactive drug use in the ancient Andes has been discovered in mummies' hair, a new study says.

The finding confirms that predecessors of the Inca known as the Tiwanaku used mind-altering substances, and hints that the civilization relied on far-reaching trade networks to obtain the drugs.

Scientists recently analyzed 32 naturally mummified Tiwanaku bodies discovered in northern Chile's Azapa Valley, which lies in the Atacama Desert.

The researchers discovered a compound called harmine in hairs from an adult male and a one-year-old baby, who both date to sometime between A.D. 800 and 1200. Harmine can help humans absorb hallucinogens and may be a powerful antidepressant.

"These individuals probably ingested harmine in therapeutic or medicinal practices, some maybe related to pregnancy and childbirth," said study co-author Juan Pablo Ogalde, a chemical archaeologist at the University of Tarapacá in Arica, Chile.

"However, it is possible also that consumption of harmine was involved in religious rituals, said Ogalde, whose research appeared online October 14 in the *Journal of Archaeological Science*.

X-rays showed that the adult male—who was buried with items of social prestige such as panpipes, a four-pointed hat, and a snuffing tray—had damage near the nose, perhaps from sniffing.

As for the baby, Ogalde speculated that the mother had consumed the drug and passed it on to her offspring during pregnancy or breast-feeding.

"The fact this mind-altering substance was found even with a one-year-old shows how much a part of their life it was," said archaeologist Alexei Vranich of the University of California, Los Angeles, who did not participate in the study.

### Habitual Users

The empire of the Tiwanaku once ranged from what is now northern Chile to southern Peru. (See a map of South America.) Between roughly A.D. 500 and 1000, they expanded from their origins on the Bolivian shores of Lake Titicaca via religious control and military might.

Elaborately decorated snuffing kits have been found in hundreds of Tiwanaku tombs. Archaeologists think these trays and tubes were used to inhale herbs, perhaps ceremonially.

Some snuff kits have been found bearing powder from the vilca tree, whose seeds are rich in hallucinogens. Also, X-rays of Tiwanaku skulls have in many cases revealed nasal damage that was likely caused by frequent sniffing.

The incorporation of snuffing imagery into Tiwanaku ceramics, woodwork, stonework, and textiles have been seen to suggest that snuffing rituals played an important role in Tiwanaku culture.

Still, no traces of hallucinogens had been found in Tiwanaku mummies until now, perhaps because the compounds broken down over time.

### Drug Trade

The only plant in South America known to contain harmine is the jungle vine *Banisteriopsis caapi*, which is used by modern-day Amazonian natives to help make an infusion known as ayahuasca for shamanic rituals.

[\*\(Read more about ayahuasca.\)\*](#)

This rain forest plant does not grow along the Atacama coast, suggesting extensive trade networks that brought the vine from as far as the Amazon rainforest. The Amazon is roughly 300 miles (500 kilometers) from the Azapa Valley, study co-author Ogalde said.

"A lot of people had suggested contact across the Amazon and the Atacama desert, and it's nice to have more hard data for that theory," said UCLA's Vranich.

The Tiwanaku may have actively searched for exotic hallucinogens to draw others to their culture, Vranich said.

"One of the sources of the mystique of the Tiwanaku—one of the reasons a lot of people may have subscribed to their religion—would have been such a mind-altering substance," he explained.

"It would have been a tremendous draw, especially when the rest of normal life in the rural Andes during that period would have been comparatively quite mundane and dull."



## Russians the first potters on earth?

Russian archeologists claim that the Russians were the first people on the planet to cultivate land, breed cattle and make earthenware.

Russian tribes inhabited Khabarovsk Region in the Stone Age, the archeologists said after finding a 15,000-year-old hunters' settlement on the bank of the Amur River in Khabarovsk.

Stone axes, knives, scrapers, arrowheads and baked earthenware have so far been unearthed in the area.

"It was the first earthenware on the globe, and though it was primitive, with plain decoration, and poorly baked, yet it was a significant landmark in the history of mankind," said Andrei Malyavin, an employee of Khabarovsk Archeology Museum.

Firing shaped clay is among the possible first steps toward social organization, or society. The production of earthenware shows that the group had moved beyond simple farming, and into some specialization.

Khabarovsk is the administrative center and the largest city of Khabarovsk Krai, Russia, located some 30 km from the Chinese border. *HRF/JG/RA*



## New hope for multiple sclerosis sufferers

### ***Research indicates drug not only stops the disease from advancing but may also restore lost function in many patients***

A drug which was developed in Cambridge and initially designed to treat a form of leukaemia has also proven effective against combating the debilitating neurological disease multiple sclerosis (MS).

The study, led by researchers from the University of Cambridge, has found that alemtuzumab not only stops MS from advancing in patients with early stage active relapsing-remitting multiple sclerosis (RRMS) but may also restore lost function caused by the disease. The findings were published today in the *New England Journal of Medicine*.

Alemtuzumab has a long connection with Cambridge, England. In 1984, Cambridge scientist Cesar Milstein was awarded the Nobel Prize for Physiology or Medicine, jointly with George Kohler, for inventing the technology to make large quantities of a desired type of monoclonal antibody. Further work in Cambridge, by Herman Waldmann and Greg Winter, led to the production of the first humanised monoclonal antibody for use as a medicine, Campath-1H, now known as alemtuzumab. It has been licensed for the treatment of chronic lymphocytic leukaemia, and has also been tested in several diseases where the immune system is overactive, such as multiple sclerosis.

The new study, which was funded by Genzyme and Bayer Schering Pharma AG, Germany, found that alemtuzumab reduces the number of attacks experienced by people with relapsing-remitting multiple sclerosis by 74 per cent over and above that achieved with interferon beta-1a, one of the most effective licensed therapies for similar cases of MS. More importantly, alemtuzumab also reduced the risk of sustained accumulation of disability by 71 per cent compared to interferon beta-1a.

Additionally, the investigators showed that many individuals in the trial who received alemtuzumab recovered some of their lost functions and so were less disabled after three years than at the beginning of the study, in contrast to worsening disability in the interferon beta-1a treated patients. These findings suggest that alemtuzumab may allow damaged brain tissue to repair, enabling the recovery of neurologic functions lost following poor recovery from previous MS attacks.

The new research shows that alemtuzumab is a much more effective treatment for early-stage RRMS than the currently approved drug interferon beta-1a. However, as the study was a Phase 2 clinical trial, additional research will need to be conducted before the drug is considered for approval in the treatment of MS.

"Alemtuzumab is the most promising experimental drug for the treatment of multiple sclerosis, and we are hopeful that the Phase 3 trials will confirm that it can both stabilize and allow some recovery of what had previously been assumed to be irreversible disabilities," says the principal investigator Alastair Compston, Professor of Neurology and the Head of the Department of Clinical Neurosciences at the University of Cambridge.

Multiple sclerosis is an autoimmune disease which is caused by the body's immune system attacking nerve fibres and their protective insulation, the myelin sheath, in the central nervous system. This damage prevents the nerves from 'firing' properly, and then leads to their destruction, resulting in physical and intellectual disabilities. Alemtuzumab works by destroying one population of white blood cell (lymphocytes) and, by shutting down the immune system, inhibits the damage to brain tissue that occurs in MS.

"The ability of an MS drug to promote brain repair is unprecedented. We are witnessing a drug which, if given early enough, might effectively stop the advancement of the disease and also restore lost function by

promoting repair of the damaged brain tissue," says Dr Alasdair Coles, University Lecturer at the Department of Clinical Neurosciences, University of Cambridge who coordinated many aspects of the study.

The main side effect of treatment is, paradoxically, that people can develop other autoimmune diseases as the immune system gradually recovers following exposure to alemtuzumab. During the trial, 20% of people treated with alemtuzumab developed an over- or under-active thyroid gland. Rarely (3%) people developed a low platelet count and were vulnerable to bleeding. This complication led to one fatality during the trial. Although potentially very serious, this complication can be easily treated if recognised early.

The Phase 2 clinical study involved 334 patients who had been diagnosed with early-stage RRMS but had not previously been treated. Patients either received alemtuzumab (one of two dose levels intravenously for five days initially and three days of re-treatment 12 months later) or interferon beta-1a (given by injection three times per week). The patients were followed for three years to determine the efficacy of the treatments as well as the effect on the patients' disabilities.

MS affects almost 100,000 people in the United Kingdom, 400,000 in the United States and several million worldwide. Symptoms of the disease can include loss of physical skills, sensation, vision, bladder control, and intellectual abilities.

#### **Notes to Editors:**

1. The paper, '*Alemtuzumab versus Interferon beta-1a in Early, Relapsing-Remitting Multiple Sclerosis*', is published in the 23 October 2008 edition of the *New England Journal of Medicine*.

2. *History of alemtuzumab and Cambridge: Alemtuzumab (previously known as Campath-1H) was first created by academics at Cambridge University in the late 1970s. The drug was shown to be useful in treating leukemia by killing the cancerous white cells of the immune system. It was also used experimentally to treat autoimmune diseases, where the white cells of the immune system are not cancerous but are targeting and damaging normal parts of the body. It was believed that a 'short sharp shock' to the immune system by alemtuzumab would re-educate' the immune system and stop it from fighting the healthy tissues in the body.*

### **UCSB study finds physical strength, fighting ability revealed in human faces**

(Santa Barbara, Calif.) — For our ancestors, misjudging the physical strength of a would-be opponent might have resulted in painful — and potentially deadly — defeat.

Now, a study conducted by a team of scientists at the University of California, Santa Barbara has found that a mechanism exists within the human brain that enables people to determine with uncanny accuracy the fighting ability of men around them by honing in on their upper body strength. What's more, that assessment can be made even when everything but the men's faces are obscured from view. A paper highlighting the researchers' findings appears in the current issue of the *Proceedings of the Royal Society*.

"Assessing fighting ability was important for our ancestors, and the characteristic that the mind implicitly equates with fighting ability is upper body strength," said Aaron Sell, a postdoctoral fellow at UCSB's Center for Evolutionary Psychology and the paper's lead author. "That's the component of strength that's most relevant to premodern combat. The visual assessment of fighting ability is almost perfectly correlated with the perception of strength, and both closely track actual upper body strength. What is a bit spooky is that upper body strength can even be read on a person's face.

Sell conducted the study with Leda Cosmides, a professor of psychology and co-director of the Center for Evolutionary Psychology; John Tooby, a professor of anthropology and also co-director of the Center for Evolutionary Psychology; Michael Gurven, an associate professor of anthropology; and graduate students Daniel Sznycer and Christopher von Rueden.

The study consisted of four sections, each of which asked the test subjects to assess the physical strength of individuals based on photographs of their faces, their bodies, or both. Subjects were asked to rank the physical strength or fighting ability of the people in the photographs on a scale of one to seven. When the photographs depicted men whose strength had been measured precisely on weight-lifting machines, the researchers found an almost perfect correlation between perceptions of fighting ability and perceptions of strength. "When you see that kind of correlation it's telling you you're measuring the same underlying variable," said Tooby.

They also found that perceptions of strength and fighting ability reflected the target's actual strength, as measured on weight-lifting machines at the gym. In other sections of the study, the researchers showed that this result extended far beyond the gym. Both men and women accurately judge men's strength, whether those men are drawn from a general campus population, a hunter-horticulturalist group in Bolivia, or a group of herder-horticulturalists living in the Argentinian Andes.

Leg strength was measured along with upper body strength in both the United States and Bolivian populations, but the results showed that perceptions of men's strength and fighting ability reflect upper body strength, not that of legs. "That makes sense," said Cosmides. "If, for example, you're trying to lift something

really heavy, or run a long distance, your lower body — your legs — will also be significant. But for fighting at close quarters, it's the upper body that really matters."

Added Tooby: "Whether people are assessing toughness or strength, it's upper body strength they implicitly register. And that's the critical information our ancestors needed in deciding — or feeling — whether to surrender a disputed resource or escalate aggressively."

The researchers suggest that the ability to judge physical strength and fighting ability serves different, but equally important, purposes for men and women. In men, the mechanism is a barometer for measuring potential threats and determining how aggressive or submissive they should be when facing a possible enemy. For women, the mechanism helps identify males who can adequately protect them and their children. Men have a lot more experience with rough and tumble play and direct experience with fighting, yet women are just as good at assessing these variables. The authors also point out that neither men nor women fare as well in assessing women's strength. This is entirely expected because, ancestrally, inflicting violence was mostly the province of men.

"The next step is to isolate what it is in the face that indicates upper body strength," said Sell. He suggests that the correlation may lie in the heavier brow ridge and thicker jaw that result from increased levels of testosterone. "Many studies have been done on the effects of testosterone on the face. There's a good chance testosterone is involved in regulating the body for battle, and men with high testosterone — those with a heavy brow ridge and thicker jaw — developed bodies that were more prepared for combat."

"One reason we evolved the ability to perceive physical strength in the face may be that it's where we focus our attention when we look at someone," said Cosmides.

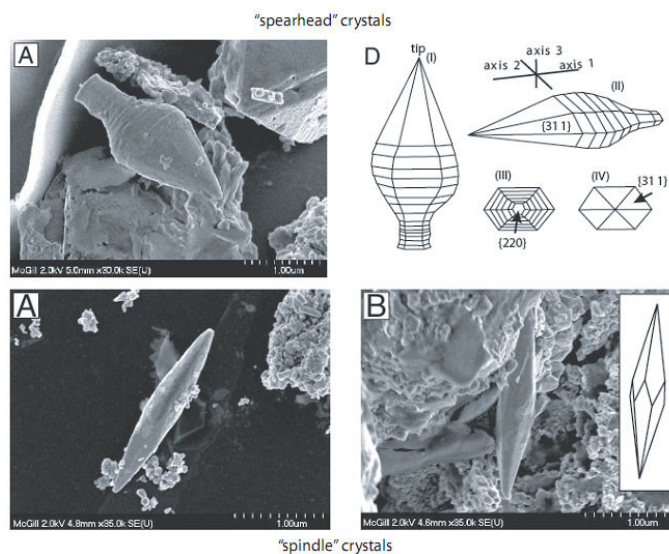
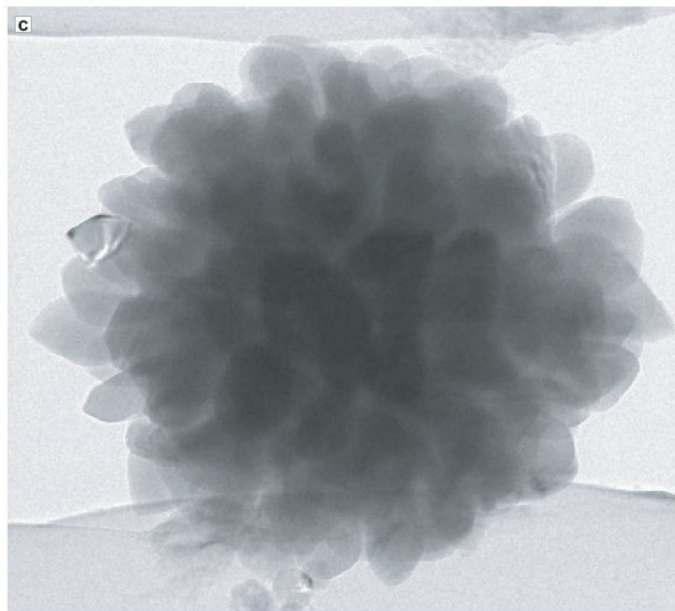
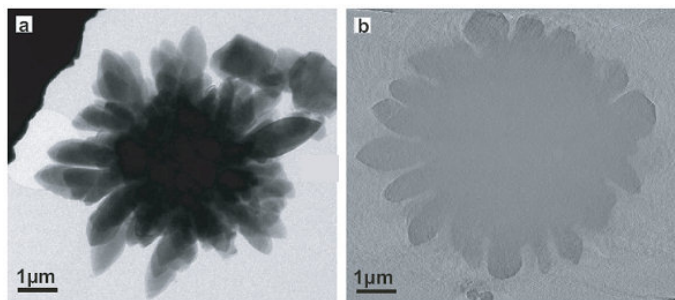
"Even if we are able to see someone's body, we always look at the face. It's so rich in social information — what a person is thinking or feeling — and adding the assessment of physical strength is a huge benefit. A person who is angry and strong offers a much greater threat than the person who is angry but weak."

### Caltech Geobiologists Discover Unique "Magnetic Death Star" Fossil Fossil and other new forms date to ancient period of global warming

PASADENA, Calif.-- An international team of scientists has discovered microscopic, magnetic fossils resembling spears and spindles, unlike anything previously seen, among sediment layers deposited during an ancient global-warming event along the Atlantic coastal plain of the United States.

The researchers, led by geobiologists from the California Institute of Technology (Caltech) and McGill University, describe the findings in a paper published online this week in the Proceedings of the National Academy of Sciences (PNAS).

Fifty-five million years ago, Earth warmed by more than 9 degrees Fahrenheit after huge amounts of carbon entered the atmosphere over a period of just a few thousand years. Although this ancient global-warming episode, known as the Paleocene-Eocene Thermal Maximum (PETM), remains incompletely explained, it might offer analogies for possible global warming in the future.



Perhaps in response to the environmental stress of the PETM, many land mammals in North America became dwarfed. Almost half of the common sea bottom-dwelling microorganisms known as foraminifera became extinct in newly warmer waters that were incapable of carrying the levels of dissolved oxygen for which they were adapted.

"Imagine our surprise to discover not only a fossil bloom of bacteria that make iron-oxide magnets within their cells, but also an entirely unknown set of organisms that grew magnetic crystals to giant sizes," said Caltech postdoctoral scholar Timothy Raub, who collected the samples from an International Ocean Drilling Program drill-core storehouse at Rutgers University in New Jersey.

A typical "giant" spearhead-shaped crystal is only about four microns long, which means that hundreds would fit on the period at the end of this sentence. However, the crystals found recently are eight times larger than the previous world record for the largest bacterial iron-oxide crystal.

According to Dirk Schumann, a geologist and electron microscopist at McGill University and lead author of the study, "It was easy to focus on the thousands of other bacterial fossils, but these single, unusual crystals kept appearing in the background. It soon became evident that they were everywhere."

In addition to their unusually large sizes, the magnetic crystals occur in a surprising array of shapes. For example, the spearhead-like crystals have a six-sided "stalk" at one end, a bulbous middle, and a sharp, tapered tip at the other end. Once reaching a certain size, spearhead crystals grow longer but not wider, a directed growth pattern that is characteristic of most higher biological organisms.

The spearhead magnetic crystals compose a minor fraction of all of the iron-oxide crystals in the PETM clay layer. Most of the crystals have smaller sizes and special shapes, which indicate that they are fossils of magnetotactic bacteria. This group of microorganisms, long studied at Caltech by study coauthor Joseph Kirschvink, the Nico and Marilyn Van Wingen Professor of Geobiology, use magnets to orient themselves within Earth's magnetic field, and proliferate in oxygen-poor water.

Spearheads are not, however, the rarest fossil type in the deposit. That honor belongs to a spherical cluster of spearheads informally dubbed the "Magnetic Death Star" by the researchers. The Magnetic Death Star may have preserved the crystals as they occurred in their original biological structure.

The researchers could not find a similar-shaped organism anywhere in the paleontological annals. They hypothesize that it may have been a single-celled eukaryote that evolved for the first time during the PETM and was outcompeted once the strange climate conditions of that time diminished. Alternatively, it may still exist today in a currently undiscovered location.

"The continental shelf of the mid-Atlantic states during the PETM must have been very iron-rich, much like the Amazon shelf today," notes study coauthor Robert Kopp of Princeton University, who first started working on the project while a graduate student at Caltech. "These fossils may be telling a story of radical environmental transformation: imagine a river like the Amazon flowing at least occasionally where the Potomac is today." *The paper, "Gigantism in unique biogenic magnetite at the Paleocene-Eocene Thermal Maximum," will appear in the early online issue of PNAS the week of October 20. The Caltech work was supported by the NASA Exobiology program.*

### **Half-feathered dinosaur was a bit of a show-off**

\* 12:25 23 October 2008

\* NewScientist.com news service

\* **Jeff Hecht**

A pigeon-sized, flightless dinosaur that may have lived before Archaeopteryx had a body covered with short downy feathers and four spectacular display feathers on its tail.

The Chinese fossil, named Epidexipteryx (meaning "display feather"), "is very close to the bird lineage," says Fucheng Zhang of the Institute of Vertebrate Palaeontology and Palaeoanthropology in Beijing, China.

The creature's evolutionary relationships to other dinosaurs, its age, and some details of its anatomy remain uncertain. Epidexipteryx might have evolved from flying ancestors, Zhang says, but its age and appearance suggest "that display feathers appeared before airfoil feathers and flight ability".

The fossil's most striking features are four ribbon-like tail feathers stretching at least 20 centimetres – the full length is uncertain as the tips are no longer present. Parallel filaments resembling the barbs in bird feathers run along their length.

*Reconstruction of Epidexipteryx (Image: Qiu Ji and Xing Lida)*



邱进 邢立达 复原  
Reconstructed by Qiu Ji & Xing Lida

The shoulders show short fuzzy feathers, which Zhang says also covered the body. But its limbs show no trace of flight feathers.

### **Intermediate stage**

The closest known relative of the new find is Epidendrosaurus, the only known specimen of which is a smaller, juvenile dinosaur with a 30-cm bony tail that is about three times its body length.

The two came from the same deposits, and are so similar that Tom Holtz of the University of Maryland first thought the new find was a more mature Epidendrosaurus.

However, the tail of the new find is much shorter, and Zhonghe Zhou of IVPP calls it "a sub-adult stage of a close relative instead of an adult of Epidendrosaurus".

Zhang assigns the two little dinosaurs to a group called Scansoriopterygidae (meaning "climbing wings"), a close cousin of the group that includes Archaeopteryx and all later birds. That places it between flying birds and clearly flightless feathered dinosaurs such as the oviraptorosaurs and dromeosaurs.

The Epidexipteryx fossil comes from the Daohugou formation in Inner Mongolia, recently dated at 152 to 168 million years, which makes it slightly older than Archaeopteryx.

Its age remains controversial, but "time is not critical," says Phil Senter of Fayetteville State University in North Carolina. "It might be a more primitive species that lingered" after Archaeopteryx evolved.

*Journal reference: Nature (DOI: 10.1038/nature07447)*

### **With hot coffee, we see a warm heart, Yale researchers find**

New Haven, Conn. - Our judgment of a person's character can be influenced by something as simple as the warmth of the drink we hold in our hand.

In the current issue of the journal *Science*, Yale University psychologists show that people judged others to be more generous and caring if they had just held a warm cup of coffee and less so if they had held an iced coffee. In a second study, they showed people are more likely to give something to others if they had just held something warm and more likely take something for themselves if they held something cold.

The study builds upon earlier work by the authors that shows the physical distance between individuals also influences their social judgments about another person.

The research suggests that saying that someone is warm or that you feel distant from a friend or relative are more than simple metaphors. They are literal descriptions of emotions such as trust, first experienced during the intimate bond formed between mother and child during infancy.

"When we ask whether someone is a warm person or cold person, they both have a temperature of 98.6 " said John A Bargh, a professor of psychology at Yale and co-author of the paper with Lawrence E. Williams of the University of Colorado who received his Ph.D. from Yale earlier this year. "These terms implicitly tap into the primitive experience of what it means to be warm and cold."

Psychologists have long noted the importance of warm physical contact with caregivers in developing healthy relationships as adults. So Bargh and Williams decided to test the impact of warmth on the perceptions of adults.

To test their hypothesis about the importance of temperature, research assistants casually asked that the undergraduate test subjects briefly hold either a warm cup of coffee or iced coffee as they wrote down information. The subjects were then given a packet of information about an individual and then asked to assess his or her personality traits. The participants assessed the person as significantly "warmer" if they had previously held the warm cup of coffee rather than the iced cup of coffee. On personality scales unrelated to the trait of "warmth," the researchers found no difference in how participants who held an iced, versus hot, coffee responded.

In the second study, participants held heated or frozen therapeutic packs as part of a product evaluation study and were then told they could receive a gift certificate for a friend or a gift for themselves. Those who held the hot pack were more likely to ask for the gift certificate, while those who held the frozen pack tended to keep the gift.

"It appears that the effect of physical temperature is not just on how we see others, it affects our own behavior as well," Bargh said. "Physical warmth can make us see others as warmer people, but also cause us to be warmer – more generous and trusting – as well."

The demonstration of the power of temperature on character assessment has been supported by recent brain imaging studies, Bargh noted. For instance, the experience of hot or cold stimulus has been shown to trigger strong activity in the insular cortex. Researchers have also implicated the same area of the brain in borderline personality disorder, a debilitating illness characterized by an inability to cooperate and near complete inability to determine whom to trust.

## 'Fart gas' link to blood pressure

The gas best known for being used in many stink bombs may also control blood pressure, say US researchers.

Small amounts of hydrogen sulphide - a toxic gas generated by bacteria living in the human gut - are responsible for the foul odour of flatulence. But it seems the gas is also produced by an enzyme in blood vessels where it relaxes them and lowers blood pressure. The findings in mice may lead to new treatments for high blood pressure, the Science journal reported.

Researchers at Johns Hopkins University, in Maryland, found that the gas is produced in the cells lining blood vessels by an enzyme called CSE. In mice engineered to be deficient in this enzyme, levels of hydrogen sulphide were almost depleted compared with levels in normal mice. The CSE-deficient mice also had blood pressure measurements about 20% higher than the normal mice, comparable to serious hypertension in humans.

When the engineered mice were given a drug which relaxes normal blood vessels - methacholine - there was no difference, indicating the gas is responsible for the relaxation.

### Treatments

Another gas, nitric oxide, is already known to be involved in control of blood pressure.

Researcher Dr Solomon Snyder said: "Now we know hydrogen sulphide's role in regulating blood pressure, it may be possible to design drug therapies that enhance its formation as an alternative to the current methods of treatment for hypertension."

Professor Amrita Ahluwalia, an expert in vascular pharmacology at Barts and The London Medical School, said: "This study shows that smelly hydrogen sulphide is also likely to have a role in regulating blood pressure and it will be a bit of an impetus for scientists to develop more specific tools to work out what's going on. "We know hydrogen sulphide is not good for us at high levels but it seems that at the lower levels in the body it is essential."

Dr Allan MacDonald, a reader in pharmacology at Glasgow Caledonian University, said: "Treatments based on hydrogen sulphide could become important in a variety of cardiovascular diseases," he said.

## Gladstone scientists find potential strategy to eliminate poisonous protein from Alzheimer brains

### *Inhibitor of amyloid-beta clearing enzyme found*

Scientists at the Gladstone Institute of Neurological Disease (GIND) have identified a new strategy to destroy amyloid-beta (AB) proteins, which are widely believed to cause Alzheimer's disease (AD). Li Gan, PhD, and her coworkers discovered that the activity of a potent AB-degrading enzyme can be unleashed in mouse models of the disease by reducing its natural inhibitor cystatin C (CysC).

All of us produce AB proteins in the brain. However, in most people, the proteins never build up to dangerous levels because they are cleared away by enzymes that destroy them. Previously Dr. Gan's laboratory had shown that cathepsin B (CatB) is such an AB-degrading enzyme. In the latest issue of the journal Neuron, the researchers report a highly effective approach to promote CatB-mediated clearance of AB .

"Many groups have developed drugs to block the production of AB, but the efficacy and safety of this approach remains to be demonstrated in clinical trials," said GIND Director Lennart Mucke, MD "By identifying an effective strategy to enhance the removal of AB, this research provides a very promising alternative or complementary therapeutic avenue."

High levels of AB in the brain may result from overproduction of AB or from an inability to eliminate it from the brain. While most work has focused on the first option, the latter has been problematic. For example, efforts to develop a vaccine that would trigger the immune system to eliminate AB have shown limited success and resulted in adverse side effects.

"Our strategy to harness the activity of a powerful AB-degrading enzyme takes advantage of the brain's own defense system to remove the toxic AB build-up," said Dr. Gan. "In principle, one could boost the activity of CatB by expressing more of it in the brain or by reducing the activity of CysC, its natural inhibitor. We focused on the latter strategy because it has greater long-term therapeutic potential."

Many enzymes that degrade proteins are kept in check by regulators called protease inhibitors. The activity of CatB is regulated by the protease inhibitor CysC. By reducing CysC activity, the scientists were able to unleash the AB-degrading power of CatB, effectively preventing the build-up of AB in mouse models of AD.

To examine the impact of this manipulation on brain function, Dr. Gan's team measured brain cell activities that relate closely to learning and memory. Increasing CatB activity by lowering CysC levels prevented AB-induced deficits in those cellular activities. The investigators also tested the modified AD mice for learning and memory in a water maze. Higher levels of CatB activity improved the ability of AD to learn the maze and to retain the new information. Increasing CatB activity also prevented the premature mortality that is typically seen in these Alzheimer models.

"Our results suggest that CysC reduction has major therapeutic potential," Dr. Gan said. "The next step will be to develop pharmacological approaches to inhibit CysC in the human brain."

*Bingui Sun, Yungui Zhou, Brian Halabisky, Iris Lo, Seo-Hyun Cho, Nino Devidze, Sarah Mueller-Steiner, Xin Wang, and Anders Grubb also contributed to the study. The work was supported in part by the National Institute on Aging (NIA), California Department of Health and Human Services. Additional funding was provided by Hellman Family Fund and Gladstone Institutes.*

## **Port Authority to Let Commuters Buy Emissions Credits**

**By KEN BELSON**

Drivers who commute by car between New York and New Jersey can assuage their guilt by buying credits from the Port Authority of New York and New Jersey to offset their vehicles' carbon emissions.

At a board meeting on Thursday, the Port Authority announced that it had approved a measure to pay five companies a total of \$2.5 million to set up a carbon offset program for the agency.

A Web site where drivers and airline passengers can buy credits to offset carbon emissions they create will be activated in early 2009.

Money from the carbon-offset credits is typically used to plant trees, build windmills, install solar panels and take other measures that may help reduce greenhouse gas emissions.

The announcement came six months after the agency said it would establish an offset program, the first of its kind in the United States by a toll-collecting agency.

The program is part of the Port Authority's plan to become carbon neutral by 2010. The agency also wants to reduce the greenhouse gas emissions it generates by 80 percent by 2050.

"We're deeply committed to being in the national forefront in developing environmentally sustainable practices at our airports, seaports, tunnels and bridges," Anthony R. Coscia, the chairman of the Port Authority, said in a statement.

To meet its carbon emission targets, the Port Authority will make Stewart International Airport in Orange County, N.Y., a "carbon-negative" airport, install energy-efficient L.E.D. lighting at the Holland Tunnel and the George Washington Bridge, build a geothermal-powered building at Kennedy International Airport and spend \$60 million to buy and preserve environmentally sensitive land for public use.

## **US doctors regularly prescribe real drugs as placebo treatments**

***Research paper: Prescribing 'placebo treatments': results of national survey of US internists and rheumatologists***

Many rheumatologists and general internal medicine physicians in the US say they regularly prescribe "placebo treatments" including active drugs such as sedatives and antibiotics, but rarely admit they are doing so to their patients, according to a study on [bmj.com](http://bmj.com) today.

The use of placebo treatments in clinical practice has been widely criticised because it is claimed that the practice by its very nature is deceptive and therefore violates patients' autonomy. But advocates of placebo treatments argue that they could offer effective treatment for many chronic conditions without necessarily deceiving patients. Despite the controversy, to date there has been little data on doctors' attitudes towards and the use of placebo treatments in the US.

Dr Jon Tilburt and his colleagues from the National Institutes of Health as well as collaborators at Harvard and the University of Chicago examined the attitudes and behaviours to placebo treatments in a national sample of general internal medicine physicians and rheumatologists in the US.

The researchers sent a confidential survey to 1200 randomly selected practising general internal medicine physicians and rheumatologists (a group of doctors who commonly treat patients with debilitating chronic conditions that are notoriously difficult to manage medically).

The authors report that among the 679 physicians (57%) who responded to the survey half of them said they prescribed "placebo treatments" on a regular basis. Most physicians (62%) believed the practice to be ethically acceptable and were happy to recommend or prescribe placebo treatments.

The most commonly used placebo treatments prescribed in the past year were over the counter painkillers (41%) or vitamins (38%). Some of the physicians reported using antibiotics (13%) and sedatives (13%) as placebos, only 3% reported using sugar pills.

Interestingly, among those who prescribe placebo treatments, most doctors (68%) said they typically describe the placebo treatments to patients as "a potentially beneficial medicine or treatment not typically used for their condition", only rarely did they admit to explicitly describing them to patients as "placebos".

Although there was only a moderate response rate to the survey (57%), even if all the non-responders never gave placebos, placebo prescribing is still surprisingly common, say the authors.



The authors say that while the use of placebos has been controversial, the physicians in the study did not believe they were behaving unethically by either using placebos or not being upfront with their patients about doing so.

They point out that understanding the role of placebo treatments in contemporary medicine is complex. They conclude that prescribing harmless treatments like vitamins or over the counter painkillers to promote positive expectations without full disclosure of motivations might not raise alarm bells, but prescribing antibiotics and sedatives when there is no clear medical indication could have serious adverse consequences for both patients and public health.

### **New promising obesity drug may have huge potential**

According to trials, a new obesity drug, Tesofensine, which may be launched on the world market in a few years, can produce weight loss twice that of currently approved obesity drugs. The Danish company Neurosearch and a number of researchers at the Faculty of Life Sciences at University of Copenhagen are behind the promising findings.

Tesofensine can produce weight loss twice that of currently approved obesity drugs, and should be studied in phase III trials. These are the conclusions of an Article published early Online and in an upcoming edition of *The Lancet*, written by Professor Arne Astrup, Department of Human Nutrition, Faculty of Life Sciences, University of Copenhagen, Denmark, and colleagues.

Increased obesity prevalence worldwide, in both developed and developing countries, results in more people with cardiovascular disease, diabetes, musculoskeletal disorders, and cancer. Whilst gastric bypass surgery substantially reduces bodyweight and obesity-related disease, the researchers believe a treatment gap exists between the effectiveness of currently marketed obesity drugs and gastric-bypass surgery. Tesofensine – which inhibits the presynaptic uptake of the neurotransmitters noradrenaline, dopamine and serotonin in the brain – has been shown to be safe and effective in animal models. It also caused unintended weight loss when it was given obese patients with Parkinson's or Alzheimer's disease when it was researched for those conditions. The drug works by suppressing hunger, leading to an energy deficit which burns off excess body fat.

This randomised, placebo-controlled phase II study was done in five Danish obesity management centres, and involved 203 obese patients (body mass index 30-40 kg/m<sup>2</sup>), weighing a mean of just over 100kg. They were prescribed a limited-energy diet and assigned to tesofensine 0.25mg (52 patients), 0.5 mg (50), 1.0 mg (49), or placebo (52), all once daily for 24 weeks. The primary outcome was percentage change in bodyweight. A total of 161 patients completed the study, and an analysis showed that the mean weight loss recorded for placebo and diet was 2.2kg and for tesofensine 0.25mg, 0.5mg and 1.0mg it was 6.7kg, 11.3kg, and 12.8kg respectively. For the 0.5mg and 1.0mg doses, this represented a weight loss around twice that attained using sibutramine or rimonabant\*, the currently-approved therapies in Europe. Blood pressure was increased in the 1.0mg group. The most common side-effects caused by tesofensine were dry mouth, nausea, constipation, hard stools, diarrhoea, and insomnia.

The authors conclude that the 0.5mg dose of tesofensine is more promising than the 1.0mg dose because it produces a similar weight loss with less side-effects. They say: "We conclude that tesofensine 0.5 mg, once daily for 6 months, has the potential to produce twice the weight loss as currently approved drugs; however, larger phase III studies are needed to substantiate our findings."

*For more information, please contact: Professor Arne Astrup, Department of Human Nutrition, Faculty of Life Sciences, University of Copenhagen, Denmark; Tel.: office +45 3533 2476, mobile: +45 2143 3302, e-mail: ast@life.ku.dk*

*Notes to editors: \* Sibutramine has the trade name Meridia in the U.S. and Canada, Reductil in Europe and most other countries. Rimonabant is licensed in Europe and other countries as Acomplia.*

*Conflicts of interest statement: Arne Astrup receives an honorarium as a consultant and for membership of the Tesofensine Advisory Board for Neurosearch. Arne Astrup owns shares in Neurosearch A/S purchased on the stock exchange.*

### **Research identifies new link between tart cherries and risk factors for heart disease** **University of Michigan research shows 'super fruit' lowered body fat, total weight and inflammation**

CHICAGO, IL, October 26 – New research continues to link tart cherries, one of today's hottest "Super Fruits," to lowering risk factors for heart disease. In addition to lowering cholesterol and reducing inflammation, the study being presented by University of Michigan researchers at next week's American Dietetic Association annual meeting, found that a cherry-enriched diet lowered body weight and fat – major risk factors for heart disease.

In the study, at-risk, obese rats that were fed a cherry-enriched diet saw significant decreases in body weight and fat (especially the important "belly" fat with known risk for heart disease) while maintaining lean muscle mass. After twelve weeks, the cherry-fed rats had 14 percent lower body fat compared to the other rats who did not consume cherries (cherry-fed rats were approximately 54% body fat; rats eating the Western diet alone were

63% body fat). The researchers suggested cherry consumption could have an effect on important fat genes and genetic expression. According to the American Heart Association, being overweight or obese, in particular when the weight is concentrated in the middle, is a major risk factor for heart disease. Nearly two out of three Americans are overweight.

The animals were fed a "Western diet," characterized by high fat and moderate carbohydrate – in line with the typical American diet – with or without added whole tart cherry powder, as 1 percent of the diet. The study was funded by the Cherry Marketing Institute, which provided an unrestricted grant to the University of Michigan to conduct the research and was not directly involved in the design, conduct or analysis of the project.

"Heart disease is the number one killer of Americans today, so it's important we continue researching ways people can improve their diet to help reduce key risk factors," said study co-author Dr. Steven F. Bolling, a cardiac surgeon at the University of Michigan Cardiovascular Center who also heads the U-M Cardioprotection Research Laboratory, where the study was performed. "We know excess body fat increases the risk for heart disease. This research gives us one more support point suggesting that diet changes, such as including cherries, could potentially lower heart disease risk."

Cherry-enriched diets in the study also reduced total cholesterol levels by about 11 percent and two known markers of inflammation – commonly produced by abdominal fat and linked to increased risk for heart disease. Inflammation marker TNF-alpha was reduced by 40 percent and interleukin 6 (IL-6) was lowered by 31 percent. In their genetic analysis, the researchers found that the cherry-enriched diets reduced the genes for these two inflammation compounds, suggesting a direct anti-inflammation effect. While inflammation is a normal process the body uses to fight off infection or injury, according to recent science, a chronic state of inflammation could increase the risk for diseases and may be especially common for those who are overweight or obese, at least in part because of excess weight around the middle. Researchers say the animal study is encouraging and will lead to further clinical studies in humans to explore the link between diet, weight, inflammation and lowering heart disease risk.

### **The Power of Eating Red**

Tart cherries, frequently sold as dried, frozen or juice, contain powerful antioxidants known as anthocyanins, which provide the bright, rich red color. Studies suggest these colorful plant compounds may be responsible for cherries' anti-inflammatory properties and other health benefits.

This new research is the latest linking this red hot "Super Fruit" to protection against heart disease and inflammation. In fact, research suggests the red compounds in cherries that deliver the anti-inflammatory benefits may also help ease the pain of arthritis and gout. There have been more than 65 published studies on the potential health benefits which can be found in the Cherry Nutrition Report posted on [www.choosecherries.com](http://www.choosecherries.com).

*Source: Seymour EM, Lewis A, Kirakosyan A, Bolling S. The Effect of Tart Cherry-Enriched Diets on Abdominal Fat Gene Expression in Rats. American Dietetic Association FNCE 2008.*

### **Deprived of a sense of smell, worms live longer**

Many animals live longer when raised on low calorie diets. But now researchers at Washington University School of Medicine in St. Louis have shown that they can extend the life spans of roundworms even when the worms are well fed — it just takes a chemical that blocks their sense of smell.

Three years ago, the researchers, led by Kerry Kornfeld, M.D., Ph.D., reported they found that a class of anticonvulsant medications made the roundworm *Caenorhabditis elegans* live longer. But until now, they didn't quite know what the drugs did to give the worms their longevity. They report their latest findings in the Oct. 24 issue of the Public Library of Science Genetics.

"We've learned that the drugs inhibit neurons in the worm's head that sense chemicals in their surroundings — the neurons are like the worm's nose," says Kornfeld, professor of developmental biology. "Like roundworms that are grown in a food-scarce environment, the worms exposed to the anticonvulsant ethosuximide lived longer. But these worms ate plenty of food. That suggests that the worms' sensation of food is critical to controlling their metabolism and life span."

If roundworms sense that food is abundant, their metabolism adjusts accordingly. Their bodies respond to promote rapid ingestion, rapid growth and rapid aging, Kornfeld explains. In contrast, when the worms sense a shortage of food, they make "metabolic decisions" to delay growth, delay energy use and extend lifespan.

In the long term, Kornfeld's goal is to identify compounds that could potentially delay human aging. The research group for this project also included James Collins, Ph.D., Kim Evason, M.D., Ph.D., Chris Pickett, Ph.D., and Daniel Schneider.

Kornfeld's lab studies *C. elegans* because they live only about two to three weeks, so experimental results can be obtained quickly. In addition, the worms' genome has been sequenced and extensively studied.

The scientists' strategy has been to expose the roundworms to libraries of chemicals to identify compounds that delay aging and extend their lives. That approach led to the unexpected result that some human anticonvulsants slow aging in *C. elegans*.

Now, further investigating the effect of one of those compounds, ethosuximide, the researchers found that it had the same life-extending effect as some well-studied genetic mutations in *C. elegans*. These mutations inhibit the activity of some sensory neurons in the worm, and that helped the researchers conclude that ethosuximide also directly affected these neurons. Roundworms treated with ethosuximide lived up to 29 percent longer than normal.

"Now we know what cells ethosuximide targets in *C. elegans*," Kornfeld says. "It's likely that the drug prevents the nerve cells from being electrically active, but precisely how it does that is something we need to study further. We also want to find out how the effect on the neurons is translated into an effect on the worms' bodies to delay aging."

Ethosuximide is used to treat seizure disorders in people. Interestingly, a common side effect of the drug is the loss of the sense of taste. Does that mean the ability to taste or smell food affects aging in people? It's probably not that simple, but it does hint at some sort of connection, Kornfeld says. He says it's possible that sensory perception cues have important metabolic consequences independent of what we actually eat.

"Emerging evidence suggests that core metabolic pathways that modulate lifespan in worms also modulate lifespan in vertebrates such as mice and perhaps humans," Kornfeld says. "Sensory pathways might also be fairly universal. In an ancient common ancestor, these pathways might have caused metabolic adjustments that affect lifespan. That could be reflected in our own biology."

*Collins JJ, Evason K, Pickett CL, Schneider DL, Kornfeld K. The anticonvulsant ethosuximide disrupts sensory function to extend C. elegans lifespan. Public Library of Science Genetics. Oct. 24, 2008.*

### **The risk factors of idiopathic pulmonary fibrosis in HCV patients**

Hepatitis C virus (HCV) is one of the more common causes of chronic liver disease in world with a variety of extrahepatic complications such as essential mixed cryoglobulinemia, membranoproliferative glomerulonephritis, autoimmune thyroiditis, sialadenitis, and cardiomyopathy. IPF is present in patients with chronic HCV infection. However, there is little or no information on the yearly cumulative incidence and risk factors on the development rate of IPF in patients with HCV.

A research team led by Yasuji Arase from Toranomon Hospital of Japan addresses this question and this will be published on October 14, 2008 in the World Journal of Gastroenterology. In this study, they studied 6150 HCV infected patients who were between 40-70 years old (HCV-group). Another 2050 patients with hepatitis B virus (HBV) were selected as control (HBV-group). The mean observation period was  $8.0 \pm 5.9$  years in HCV-group and  $6.3 \pm 5.5$  years in HBV-group.

They found that fifteen patients in HCV-group developed IPF. On the other hand, none of the patients developed IPF in HBV-group. In HCV-group, the cumulative rates of IPF development were 0.3% at 10th year and 0.9% at 20th year. The IPF development rate in HCV-group was higher than that in HBV-group ( $P = 0.021$ ). The IPF development rate in patients with HCV or HBV was high with statistical significance in the following cases: (1) patients  $\geq 55$  years ( $P < 0.001$ ); (2) patients who had smoking index (package per day  $\times$  year) of  $\geq 20$  ( $P = 0.002$ ); (3) patients with liver cirrhosis ( $P = 0.042$ ). This result indicated that age, liver cirrhosis and smoking enhance the development of IPF in patients with chronic hepatitis C infection.

**Reference:** Arase Y, Suzuki F, Suzuki Y, Akuta N, Kobayashi M, Kawamura Y, Yatsuji H, Sezaki H, Hosaka T, Hirakawa M, Saito S, Ikeda K, Kumada H. Hepatitis C virus enhances incidence of idiopathic pulmonary fibrosis. *World J Gastroenterol* 2008; 14(38): 5880-5886 <http://www.wjgnet.com/1007-9327/14/5880.asp>

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### **When did the Earth turn green?**

\* 16:00 23 October 2008

\* NewScientist.com news service

\* **Rachel Nowak**

Photosynthesis – the process by which organisms like plants convert light energy into chemical energy – may not have been around quite as long as previously thought.

That's the conclusion of a study of solidified oil that formed around 2.7 billion years ago in the Pilbara region of Western Australia.

The study, led by Birger Rasmussen of the Curtin University of Technology in Perth, means the planet had to wait another 550 million years for photosynthesis to get going, and that the oldest known eukaryotic (complex) cells are one billion years younger than previously thought.

"A lot of people will revisit their understanding of the late Archaean period in light of these results," says Woodward Fischer of the California Institute of Technology, Pasadena.

### **Oxygen surge**

Photosynthesis converts carbon dioxide and water into carbohydrates and oxygen. The process is the most likely explanation for "the great oxidation" event 2.4 billion years ago, when oxygen in the atmosphere started to build up, paving the way for the evolution of complex life-forms like animals.

The oxygen surge is also considered to be the strongest clue to the timing of the evolution of photosynthesis. But until now it has conflicted with the fossil evidence.

Almost a decade ago, Jochen Brocks, then at the University of Sydney, found minute traces of organic molecules that could only have come from photosynthetic cyanobacteria in Pilbara shale (*Science*, vol 285, 1033). Other organic molecules were indicative of eukaryotic cells.

At the time, Brocks' analysis dated the so-called "molecular fossils" at 2.7 billion years ago.

### **Not so old**

But the new evidence from the Rasmussen team suggests that what Brocks had found was actually molecular contaminants from a more recent era. Brocks is a co-author of the Rasmussen paper.

"The existing unambiguous fossil evidence for the timing of photosynthesis now moves to 2.15 billion years ago," says Rasmussen, referring to fossilised cyanobacteria that have been found in Canada's Belcher Islands.

Rasmussen, Brocks and their colleagues used a relatively new device called a NanoSIMS ion probe to monitor the types of carbon isotopes in solidified oil – the proposed source of Brocks' organic compounds – in the bits of rock left over from the original study.

"The oil had to have formed in the rock, but its isotopic signature was completely different to that of the microbial fossils, so we concluded that the microbial fossils were more recent contaminants," says Rasmussen.

### **Not done yet**

Other paradoxes remain to be solved, however. Since Brocks' discovery a decade ago, "molecular fossils" of photosynthesis from before 2.4 billion years ago have turned up at other sites.

"We suspect that those studies will turn out to be flawed, too," says Rasmussen.

*Journal reference: Nature, DOI: 10.1038/nature07381*

## **Female Plant 'Communicates' Rejection or Acceptance of Male**

### ***MU researcher identifies pollen proteins that provide insight into the fertilization process***

Oct. 23, 2008 Story Contact: **Kelsey Jackson**, (573) 882-8353, JacksonKN@missouri.edu

COLUMBIA, Mo. – Without eyes or ears, plants must rely on the interaction of molecules to determine appropriate mating partners and avoid inbreeding. In a new study, University of Missouri researchers have identified pollen proteins that may contribute to the signaling processes that determine if a plant accepts or rejects individual pollen grains for reproduction.

Like humans, the mating game isn't always easy for plants. Plants rely on external factors such as wind and animals to bring them potential mates in the form of pollen grains. When pollen grains arrive, an introduction occurs through a "conversation" between the pollen (the male part of the flower) and the pistil (the female part of the flower). In this conversation, molecules take the place of words and allow the pollen to identify itself to the pistil. Listening in on this molecular conversation may provide ways to control the spread of transgenes from genetically-modified crops to wild relatives, offer better ways to control fertilization between cross species, and lead to a more efficient way of growing fruit trees.

"Unlike an animal's visual cues about mate selection, a plant's mate recognition takes place on a molecular level," said Bruce McClure, associate director of the Christopher S. Bond Life Sciences Center and researcher in the MU Interdisciplinary Plant Group and Division of Biochemistry. "The pollen must, in some way, announce to the pistil its identity, and the pistil must interpret this identity. To do this, proteins from the pollen and proteins from the pistil interact; this determines the acceptance or rejection of individual pollen grains."

In the study, researchers used two specific pistil proteins, NaTTS and 120K, as "bait" to see what pollen proteins would bind to them. These two pistil proteins were used because they directly influence the growth of pollen down the pistil to the ovary where fertilization takes place.

Three proteins, S-RNase-binding protein (SBP1), the protein NaPCCP and an enzyme, bound to the pistil proteins. This action suggests that these proteins likely contribute to the signaling processes that affect the success of pollen growth.

"Our experiment was like putting one side of a Velcro strip on two pistil proteins and then screening a collection of pollen proteins to see which of the pollen proteins have the complementary Velcro strip for binding," McClure said. "If it sticks, it's a good indication that the pollen proteins work with the pistil proteins to determine the success of reproduction."

In previous studies, McClure showed that S-RNase, a protein on the pistil side, caused rejection of pollen from close relatives by acting as a cytotoxin, or a toxic substance, in the pollen tube.

For their study, the MU team used *Nicotiana glauca*, a relative of tobacco commonly grown in home gardens as “flowering tobacco.” The study, “Pollen Proteins Bind to the C-Terminal Domain of *Nicotiana glauca* Pistil Arabinogalactan Proteins,” was published in the *Journal of Biological Chemistry* and was co-authored by McClure; Kirby N. Swatek, biochemistry graduate student; and Christopher B. Lee, post-doctoral researcher at the Bond Life Sciences Center.

### **Could your initials influence where you choose to work?**

#### ***A systematic test of the "name-letter effect"***

One of the most important decisions that we can make is what company we will work for. There are a number of factors to consider when making this decision, including salary, benefits and work location. However, there may also be less-obvious factors in play that sway our decision, and without us even knowing it. It is well known that unconscious thoughts can influence certain aspects of our behavior. An intriguing example of this is the “name-letter effect,” a phenomenon which shows that we have a preference for things that begin with the same letter as our first name.

Psychologists Frederik Anseel and Wouter Duyck from Ghent University (Belgium) were interested in testing the extent of the name-letter effect and if it is potent enough to affect where we choose to work. The psychologists analyzed a database containing information about Belgian employees who work full-time. More specifically, the researchers looked at the employees’ name and how often their first initial matched the first letter of their company’s name. The researchers estimated the expected number of these matches (using a probability calculation) and compared that to what they actually observed.

In a new study published in *Psychological Science*, a journal of the Association for Psychological Science, the psychologists found that there is indeed a name-letter effect between employee names and the company they work for. There were 12% more matches than was expected based on the probability estimate. The researchers noted that “hence, for about one in nine people whose initials matched their company’s initial, choice of employer seems to have been influenced by the fact that the letters matched.” In addition, when the psychologists looked across all letters, they found that this effect occurred with every letter of the alphabet, but was more apparent for rarer initials.

The authors concluded that they “have demonstrated that people are more likely to work for companies with initials matching their own than to work for companies with other initials.”

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*Related article: <http://www.psychologicalscience.org/media/releases/2007/nelson.cfm>*

### **JHU chemists devise self-assembling 'organic wires'**

From pacemakers constructed of materials that so closely mimic human tissues that a patient's body can't discern the difference to devices that bypass injured spinal cords to restore movement to paralyzed limbs, the possibilities presented by organic electronics read like something from a science fiction novel.

Derived from carbon-based compounds (hence the term "organic"), these "soft" electronic materials are valued as lightweight, flexible, easily processed alternatives to "hard" electronics components such as metal wires or silicon semiconductors. And just as the semiconductor industry is actively developing smaller and smaller transistors, so, too, are those involved with organic electronics devising ways to shrink the features of their materials, so they can be better utilized in bioelectronic applications such as those above.

To this end, a team of chemists at The Johns Hopkins University has created water-soluble electronic materials that spontaneously assemble themselves into "wires" much narrower than a human hair. An article about their work was published in a recent issue of the *Journal of the American Chemical Society*.

"What's exciting about our materials is that they are of size and scale that cells can intimately associate with, meaning that they may have built-in potential for biomedical applications," said John D. Tovar, an assistant professor in the Department of Chemistry in the Zanvyl Krieger School of Arts and Sciences. "Can we use these materials to guide electrical current at the nanoscale? Can we use them to regulate cell-to-cell communication as a prelude to re-engineering neural networks or damaged spinal cords? These are the kinds of questions we are looking forward to being able to address and answer in the coming years."

The team used the self-assembly principles that underlie the formation of beta-amyloid plaques, which are the protein deposits often associated with Alzheimer's disease, as a model for their new material. This raises another possibility: that these new electronic materials may eventually prove useful for imaging the formation of these plaques.

"Of course, much research has been done and is still being done to understand how amyloids form and to prevent or reverse their formation," Tovar said. "But the process also represents a powerful new pathway to fabricate nanoscale materials." *This research was supported by The Johns Hopkins University.*

### **Green tea may delay onset of type 1 diabetes**

**Paula Hinely** - 2008 October 23

A powerful antioxidant in green tea may prevent or delay the onset of type 1 diabetes, Medical College of Georgia researchers say.

Researchers were testing EGCG, green tea's predominant antioxidant, in a laboratory mouse with type 1 diabetes and primary Sjogren's syndrome, which damages moisture-producing glands, causing dry mouth and eyes.

"Our study focused on Sjogren's syndrome, so learning that EGCG also can prevent and delay insulin-dependent type 1 diabetes was a big surprise," says Dr. Stephen Hsu, molecular/cell biologist in the School of Dentistry.

They found it also worked well in their original disease focus.

In the mouse, EGCG reduced the severity and delayed onset of salivary gland damage associated with Sjogren's syndrome, which has no known cure.

"EGCG modulates several important genes, so it suppresses the abnormality at the molecular level in the salivary gland. It also significantly lowered the serum autoantibodies, reducing the severity of Sjogren's syndrome-like symptoms," Dr. Hsu says. Autoantibodies are antibodies the body makes against itself.

Both type 1 diabetes and Sjogren's syndrome are autoimmune diseases, which cause the body to attack itself. Autoimmune disorders are the third most common group of diseases in the United States and affect about 8 percent of the population, says Dr. Hsu. Sjogren's syndrome can occur alone or secondary to another autoimmune disease, such as lupus, rheumatoid arthritis or type 1 diabetes.

The study, published in the Oct. 24 issue of *Life Sciences*, supports earlier research showing EGCG's impact on helping prevent autoimmune disease.

Researchers treated a control group of mice with water and a test group with a purified form of EGCG dissolved in the drinking water. At 16 weeks, the EGCG-fed mice were 6.1 times more likely to be diabetes-free than the water-fed group, and 4.2 times more likely at 22 weeks.

"Previous studies used another animal model that developed type 1 diabetes only after an injected chemical killed the insulin-producing cells. That may not accurately resemble disease development in humans, because type 1 diabetes is a genetic disease," says Dr. Hsu, the study's corresponding author.

"Our study is significant because we used a mouse model with the genetic defects that cause symptoms similar to human type 1 diabetes and Sjogren's syndrome, so the immune cells attack the pancreas and salivary glands until they are no longer functional."

Another related finding was that even when salivary cells were under attack, they seemed to be rapidly reproducing in the control group. The proliferation was suppressed in the EGCG-fed group.

"It's kind of counterintuitive – why would there be proliferation of the glandular cells occurring when the present cells are not secreting saliva?" says Dr. Kevin Gillespie, first author of the study he conducted for his master's research project at MCG.

The proliferation phenomenon also can be observed in psoriasis, an autoimmune disease affecting the skin and joints, says Dr. Hsu. "Normal skin cells turn over every 30 days or so, but skin cells with psoriasis turn over every two or three days." Dr. Hsu's group previously found that green tea polyphenols, including EGCG, inhibited rapid proliferation in an animal model for human psoriasis.

"We never thought proliferation was going on to this extent in the salivary gland, but we now believe it is tightly associated with Sjogren's syndrome," he says.

The next step is to observe Sjogren's syndrome in human salivary gland samples to determine whether the study findings hold up in humans.

"If the abnormal expression of these genes is the same in humans as in the animal model, then the second stage will be intervention and treatment with a pure form of EGCG," says Dr. Hsu.

"The benefit of using green tea in preventing or slowing these autoimmune diseases is that it's natural and not known to harm the body," says Dr. Gillespie, periodontics chief resident at Fort Gordon's Tingay Dental Clinic. "EGCG doesn't have the negative side-effects that can be associated with steroids or other medications that could otherwise be prescribed."

## Cold virus found to manipulate genes

Sneezing, runny nose and chills? You might blame the human rhinovirus (HRV), which causes 30 to 50 percent of common colds. But in reality, it's not the virus itself but HRV's ability to manipulate your genes that is the true cause of some of the most annoying cold symptoms.

For the first time, researchers have shown that HRV hijacks many of your genes and causes an overblown immune response that ends up with your nose being overblown.

The research, published in the first issue for November of the American Thoracic Society's clinical research journal, the American Journal of Respiratory and Critical Care Medicine, is the first study to comprehensively review gene changes caused by HRV.

"The study's findings are a major step toward more targeted cold prevention and treatment strategies while also serving as a valuable roadmap for the broader respiratory science community," said David Proud, PhD, a professor in the Department of Physiology and Biophysics at the University of Calgary, and lead author of the study. The study was done in collaboration with scientists at the University of Virginia and the Procter & Gamble Company.

Proud added that while colds are usually considered to be minor infections of the nose and throat, they can have much more serious health repercussions. "Rhinovirus is the major cause of the common cold, but it is also an important pathogen in more serious conditions, such as asthma and chronic obstructive pulmonary disease (COPD)," he said.

"Advances in our understanding of the biology of the common cold may eventually lead to improvements in treatment or methods for prevention of colds," said Dr. Ron Turner, of the University of Virginia, one of the study's authors.

The researchers recruited volunteers who were inoculated with either HRV or a sham inoculation and obtained cell scrapings from the nasal passages 8 and 48 hours after inoculation and assessed the genetic changes by microarray, also known as gene chip technology.

After 8 hours, there were virtually no differences between the control and the HRV-inoculated group, but by the 48-hour mark, more than 6500 genes had been significantly up- or down-regulated in the HRV subjects—many of the more highly up-regulated genes fell into two major categories: genes making antiviral proteins, including viperin; or genes making pro-inflammatory cytokines.

"This is the first comprehensive picture to identify several groups of genes that are likely to contribute to the pro-inflammatory and antiviral response," said Dr. Proud.

The researchers also found that viral titer more than doubled in cells that had had the viperin-producing gene "knocked down," showing that HRV replication was hampered by viperin. "This had never been examined during rhinovirus infections," said Dr. Proud. "Some evidence existed that this protein (only discovered a few years ago) had effects on influenza, but nothing was known about its role in rhinovirus infections. So it was a bit unexpected."

"Overall these data provide new insights into the host response to HRV infection and identify several novel candidate genes that require further study to clarify their role in disease pathogenesis," said Dr. Proud. "This may identify proinflammatory, or host defense pathways that could be targeted for drug development, not only as treatments for colds but also for viral exacerbations of asthma and COPD."

The fact that genes associated with structural 'remodeling' of the airways were also altered, supports further study of the role of rhinovirus infections in airway remodeling in asthma."

*Full text of original article available here: <http://www.thoracic.org/sections/publications/press-releases/resources/110108Proud.pdf>*

## Phony Friends? Rejected People Better Able to Spot Fake Smiles

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"There are hundreds of languages in the world, but a smile speaks them all." It's true too—next time you are lost in a foreign country, just flash a smile and the locals will be happy to help you find your way. An honest smile can convey a wide range of meanings, from being happy to having fun. Although, not all smiles are genuine. All of us have "faked a smile" at some point.

Now, a new study might make us think twice about sending out a phony grin. It has been shown that individuals who are experiencing rejection are better at picking up subtle social cues and according to a recent study published in the October issue of Psychological Science, a journal of the Association for Psychological Science, socially rejected people are particularly good at discerning fake smiles from real ones.

Psychologist Michael J. Bernstein and his colleagues from Miami University wanted to see to what extent rejected individuals would be able to identify the authenticity of a facial expression. The researchers induced feelings of social rejection in a group of the participants by making them think about a time when they felt

socially isolated. Conversely, another group of participants were asked to recall times they felt accepted or included in a group. A control group of participants were asked to recall the previous morning's activities (resulting in neutral feelings). The participants then viewed videos of people smiling—some of the videos showed people expressing genuine smiles and the rest depicted people with fake smiles. Participants were to indicate which of the videos contained real smiles.

The results show that socially rejected individuals are better at distinguishing fake smiles from real smiles compared to individuals who feel socially accepted or who were in the control group. The authors propose that socially rejected people have an increased motivation to be accepted, thus making them more sensitive to specific social cues indicating opportunities for inclusion. The authors conclude, "It seems essential to detect legitimate signs of positivity that indicate possible reaffiliation with other people. Otherwise, rejected individuals could miss out on new chances for acceptance or 'waste' affiliation efforts on people who are not receptive."

### **World's Oldest Cooked Cereal Was Instant**

**Jennifer Viegas**, Discovery News

Oct. 24, 2008 -- European diners around 8,000 years ago could enjoy a bowl of instant wheat cereal that, aside from uneven cooking and maybe a few extra lumps, wasn't very different from hot wheat cereals served today, suggests a new study that describes the world's oldest known cooked cereal.



Dating from between 5920 to 5730 B.C., the ancient cereal consisted of parboiled bulgur wheat that Early Neolithic Bulgarians could refresh in minutes with hot water.

***Bulgar: It's What's For Breakfast***

"People boiled the grain, dried it, removed the bran and ground it into coarse particles," lead author Soultana-Maria Valamoti told Discovery News.

"In this form, the cereal grain can be stored throughout the year and consumed easily, even without boiling, by merely soaking in hot water," added Valamoti, an assistant professor of archaeology at Aristotle University of Thessaloniki in Greece.

She and her colleagues studied the Bulgarian grain, excavated at a site called Kapitan Dimitrievo, as well as 4,000-year-old grains of barley and wheat from northern Greece. Very high magnification by microscope revealed precise details about the individual cereal grains, including their composition.

The findings are published in the latest issue of the journal *Vegetation History and Archaeobotany*.

The analysis showed that starch within the Bulgarian grains was swollen, twisted and, at times, fused together. Such starch modifications were more extreme toward the outer layers of the bulgur, consistent with grains that had been penetrated by boiling water.

The grains had also been charred -- not in a way indicative of intentional toasting, but rather by a fire that appears to have burnt down the houses where the grain was stored.

The scientists also cooked and processed modern wheat and hulled barley, putting the results through the same analysis. The fine details and internal structure of the modern boiled, dried and ground cereals matched what the researchers saw in the ancient Bulgarian grains.

"I think bulgur could have well been a staple ingredient of Mediterranean cultures in the past," Valamoti said. "It is very nutritious and easy to make a meal out of it throughout the year, once it is prepared."

She explained that the early southeastern Europeans must have gathered it in the summer, when they could have dried it under the hot sun. Such early, simple preparations passed down through the generations, leading to dishes still enjoyed in the region and other parts of the world today.

"Bulgur and trachanas (preparations often consisting of ground grain mixed with milk or yogurt) were staple foods of Greek people until very recently," she said, adding that Arabic cooks "make the wonderful tabouleh salad with bulgur," and that other sophisticated recipes using the grain later emerged.

Stefanie Jacomet, a leading archaeobotanist at Basel University's Institute of Prehistory and Archaeological Science in Switzerland, told Discovery News that "until now, simply almost nothing was known about this," explaining that this latest study is the first to explore ancient cooked cereal in such detail.

Other researchers have, however, analyzed early evidence for bread-making in the same regions. The first known bread predates the cereal, so it's possible the ancients enjoyed some toast with their hot, cooked bulgur.

Valamoti is currently working on a book that will describe early cooking methods and recipes, all of which are coming to light thanks to high-tech equipment and analysis methods.

Her family doesn't seem to mind the extensive research.

"My daughter loves bulgur," Valamoti concluded.



## Investigation of changes in properties of water under the action of a magnetic field

Professor Pang Xiao-Feng and Deng Bo studied the properties of water, and their changes under the action of a magnetic field were gathered by the spectrum techniques of infrared, Raman, visible, ultraviolet and X-ray lights, which may give an insight into molecular and atomic structures of water. It was found that some properties of water were changed, and a lot of new and strange phenomena were discovered after magnetization. Magnetized water really has magnetism, which has been verified by a peak shift of X-ray diffraction of magnetized water +Fe<sub>3</sub>O<sub>4</sub> hybrid relative to that of pure water + Fe<sub>3</sub>O<sub>4</sub> hybrid, that is, a saturation and memory effect. The study is being reported in the November 2008 issue of Science in China Series G- Physics, Mechanics & Astronomy because of its significant values in science and extensive applications in industry, agriculture and medicine.

Water is the most common and important material in nature. However, what is water on earth? What properties does water have? They are both challenging problems, and need further study. The changes in properties of water under the action of a magnetic field are also an interesting and important question, which has not been solved yet, although it has been studied for about one hundred years. So in this work, authors collected and studied the light spectra of water and its features using the spectrum techniques of light for giving an insight into the features of molecular structure in water and seeking the mechanism of magnetization of water. . These spectra may embody the features of molecular, atomic and electronic structures of water, thus giving an insight into the structures of atoms and molecules in water and providing some accurate and credible data for the features of water.

"In this work, we collect and study the light spectra of water and its features using some modern instruments and techniques, for instance, the spectrum techniques of infrared, Raman, visible, ultraviolet and X-ray lights in secs. 1 and 2. From these spectra we obtained that there are plenty of linear and closed hydrogen-bonded chains of molecules, except for free water molecules, in water, which are responsible for conductivity and magnetization of water, respectively. At the same time, a lot of new and strange properties of magnetized water, such as, the saturation and memory effect, irreversible effect of infrared absorptions, exponential increase of ultraviolet absorption, more increase of infrared absorption as well as decrease of hydrophobicity of water, were obtained. These properties are helpful to reveal the mechanism of magnetization of water. Meanwhile, we can indicate the magnetized effect of water by increment of infrared spectrum of absorption. ," noted Principal Investigator Pang Xiao-Feng, professor of University of Electronic Science and Technology of China. "This research is the first paper to carefully observe the mechanisms of magnetization of water."

In the experiments, it was found that magnetized water has an evident saturation, memory effect and magnetism through the experimental comparison of X-ray diffraction of nanoFe<sub>3</sub>O<sub>4</sub> plus magnetized water with that of nanoFe<sub>3</sub>O<sub>4</sub> plus pure water. Some new and unusual phenomena of water were also discovered, for example, the strange irreversible effect of infrared absorption in the temperature increasing and decreasing processes at high temperature, the exponential increase of ultraviolet absorption in the range of 200-300 nm and the existence of six peaks at 3037, 3165, 3280, 3415, 3540 and 3665 cm<sup>-1</sup> in the range of 3000-4000 cm<sup>-1</sup> [1-19], which do not alter with the water temperature and the externally applied fields, thus are an intrinsic feature of water.

We here investigated the variation of surface tension force and the soaking degree of water to materials through measuring the contact angles of magnetized and pure water on the surface of the materials including copper, graphite and muscovite in the range of 0°-180° under the condition of humidity of 27° using OCA40 Micro optical-vision instrument. The result shows that the magnetic field may change the hydrophobicity of water. The extenuation of contact angles of magnetized water is due to the increase of polarized effect and the changes of distribution and clustering structure of water molecules after magnetization.

Professor Pang thinks the above properties of magnetized and pure water are helpful for revealing the structural features of water molecules and verifying the correctness of the mechanism and theory of magnetization of water proposed by himself [15-19].

Based on the molecular structure of water Pang further established the theory of magnetization of water according to the theories of proton conductivity in the hydrogen bonded systems of ice [17-22] and magnetism of matter. Authors further noted: "if water is exposed in a magnetic field, these closed hydrogen-bonded chains become some ring electric-current or "molecular electric-current" elements with magnetism due to the proton conductivity in them under the action of Lorentz force of the magnetic field [19-24,25], and the magnetic interactions of these "molecular electric-current" elements with each other or with the externally applied magnetic-field result in the changes of distribution and features of water molecules and the magnetization of water". Thus these experimental results verify that Pang's theory of magnetization of water is correct and credible. In addition, there may be significant evidence if more techniques are used.

*This work is supported by the National Basic Research Program of China (973 Program)(Grant No. 2007CB936103)  
This research deserves publication because it is well written and the experimental design and method are sound. In addition, these results obtained have significant values in science and extensive applications in industry, agriculture and medicine  
The authors would like to acknowledge the experimental support from Prof. Jiang Lei and Dr. Gao Xiu-feng with Chemical Institute of Chinese Academy of Sciences, Prof. Xue We-dong with Chemical Department of Sichuan Normal University and Prof. Chen Jian with Zhong Shan University.*

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## **'New prostate' grown inside mouse**

Scientists have grown new prostate glands in mice, in another advance for stem cell technology.

The team from San Francisco were able to isolate single cells with the ability to generate an entire prostate. The technique, reported in the journal *Nature*, could shed light on how prostate tumours develop. However, any thoughts it could lead to transplants in men who have had the gland removed to beat cancer have been played down.

The prostate is found near the bladder, and helps make and expel semen, but is a common source of cancer, especially in older men.



*Prostate cancer is a major killer*

A quarter of all new cancers diagnosed in men are prostate cancers, and 10,000 die from the disease every year in the UK.

The US researchers were able to track down a type of stem cell which divides to form the different cell types in the gland. When these mouse stem cells were transplanted back into mice, they developed into entirely new glands. However, this does not mean that entirely new prostates can be fabricated for men who have lost them.

Any new gland would have to be not only connected back to the urethra - the tube which carries urine from the bladder to the outside of the body, but also somehow to the complex system of nerves controlling its activity.

Even if this complex surgery were possible, many doctors would argue that the benefits of having the gland as an older man do not entirely justify it.

### **Not needed**

Prof Robin Lovell-Badge, MRC National Institute for Medical Research, said: "Of course the main clinical problem with the prostate gland is not a need for additional ones, but their overgrowth, which often turns to prostate cancer. "However, knowing the identity of these stem cells may eventually allow the development of therapies that specifically target these cells in a way that keeps them under control."

Professor Malcolm Alison, Professor of Stem Cell Biology at Barts and The London School of Medicine and Dentistry, agreed, saying that, in older men, the prostate tended to be a cause of "serious medical problems".

"However, it is a widely held view that cancers originate from normal stem cells, so this discovery will be a significant boost to prostate cancer research aimed at understanding how this deadly disease develops."

John Neate, the chief executive of The Prostate Cancer Charity, said: "This study is an important piece in the jigsaw of our understanding of the role that stem cells play in the prostate. "It gives very clear evidence of the existence of stem cells in the prostate of mice. Scientists think they may work in a similar way in humans. "Much research is being undertaken to unravel the role stem cells may play in the development of cancer and how they may respond differently to treatments."

## **A reversal of thinking: How women with lupus can increase chance for healthy pregnancies**

### ***Hospital for Special Surgery rheumatologist provides new information to aid pregnancy in women with lupus***

In the not so distant past, women with systemic lupus erythematosus (SLE), an autoimmune disease, were advised not to have children, and if they became pregnant, to have therapeutic abortions to prevent severe flares of their lupus. Research by rheumatologists at Hospital for Special Surgery in New York, in patients with lupus who have had successful pregnancies is yielding insights that support a reversal of that thinking.

The research effort, a multi-center research initiative lead by Jane Salmon, M.D., attending physician at Hospital for Special Surgery, is known as the PROMISSE (Predictors of pRegnancy Outcome: bioMarkers In antiphospholipid antibody Syndrome and Systemic lupus Erythematosus) Study.

Two research projects will be presented at this year's American College of Rheumatology meeting in San Francisco on October 24-29 by Dr. Salmon, based on data gathered from the PROMISSE Study. She and her collaborators identified factors that help a woman and her doctor plan for a healthy pregnancy.

Patients with lupus can live free of symptoms for long periods of time and then experience a disease "flare," when symptoms such as a red rash across the nose and cheeks, painful or swollen joints, swollen legs or extreme fatigue suddenly appear. The first presentation will examine whether problems during pregnancy can be correlated to the severity, frequency and timing of disease flares. Dr. Salmon and her colleagues followed 198 pregnant patients with lupus. The investigators found that women who conceived while their disease was stable or only mildly active had relatively infrequent flares during their pregnancies and delivered healthy babies. This held true regardless of past disease severity or past kidney disease (a frequent consequence of lupus). The findings inform women with lupus on how to plan when to conceive to have a low risk pregnancy.

Lupus patients, as well as other patients with the antiphospholipid syndrome, produce special types of proteins called antiphospholipid antibodies that can attack their own tissues and cause pregnancy complications. The second study to be presented by Dr. Salmon showed that the presence of a specific subset of these autoantibodies is highly associated with poor pregnancy outcomes. Specifically, the researchers found that women who tested positive for an autoantibody called lupus anticoagulant were more likely to have complications such as miscarriage or preeclampsia during pregnancy.

These results can help doctors identify patients at high risk for complications by obtaining a blood test to determine if they are positive or negative for the lupus anticoagulant autoantibody. While women with lupus or the antiphospholipid syndrome who are positive for this protein can still have successful pregnancies, their doctors should monitor them more closely for early signs of pregnancy complications.

"Based on our new data, we believe we are in a position to help doctors counsel and care for their patients," says Dr. Salmon, Collette Kean Research Chair and co-director, Mary Kirkland Center for Lupus Research at HSS. "In the past, women were discouraged from becoming pregnant because of a very high risk to the mother and the baby. Our findings from the PROMISSE study show that women with lupus can have normal pregnancies when they work together with their doctors, beginning with the decision of when it is safe to conceive and continuing with close follow-up to anticipate potential problems."

*The PROMISSE study was funded by the National Institute of Arthritis, Musculoskeletal and Skin Diseases of the National Institutes of Health in 2003 to identify biomarkers that would predict poor pregnancy outcomes in lupus patients. To date, Dr. Salmon and the PROMISSE investigative team have enrolled 457 volunteers who are monitored with monthly checkups and research laboratory studies looking at genes and circulating proteins that may predict the course of pregnancy. After a review of the progress of and findings from the PROMISSE study, the NIH extended the funding for an additional five years, beginning with \$1.4 million for the first year of renewal, which starts in October 2008. The continued support will allow Dr. Salmon and her co-investigators from 11 academic centers to increase the number of volunteers to 700 and expand the study to examine a broader range of genes and molecular pathways that can affect pregnancy in patients with lupus, and, very probably, cause miscarriage and preeclampsia in healthy women.*

*The PROMISSE Study is coordinated by Dr. Salmon, Michael Lockshin, M.D., and Lisa Sammaritano, M.D., at Hospital for Special Surgery; Jill Buyon, M.D., at New York University School of Medicine; Ware Branch, M.D., at University of Utah Health Sciences Center; Carl Laskin, M.D., at Mt. Sinai Hospital in Toronto, Canada; Joan Merrill, M.D., at the Oklahoma*

## Runners burn more calories – even at rest

26 October 2008 NewScientist.com news service

THE benefits of exercise don't stop when the running shoes come off. A new peek inside the muscles of resting athletes shows that they burn fuel even when their bodies don't need the energy.

Endurance sports such as long-distance running are known to increase the number of mitochondria, the tiny engines inside cells that convert sugars and fats into ATP molecules, the cell's energy carriers. This boosts the capacity of muscles to consume oxygen and work at higher power during exercise.

Now Douglas Befroy and his colleagues at Yale University say that the mitochondria in the muscles of men who run at least 4 hours a week consume 54 per cent more fuel at rest than those of men who don't run (Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.0808889105). Yet the amount of ATP produced by the two sets of men was the same, indicating that when at rest the extra fuel was being "wasted", and turned into heat.

Because mitochondrial fuel-burning helps to clear out the cellular fats thought to contribute to insulin resistance, this finding suggests a way that training can help to protect against type 2 diabetes even when exercise is over.

## Purple tomatoes: The richness of antioxidants against tumors

**High anthocyanins content tomatoes, produced by European researchers, may be able to extend lifespan in cancer-prone mice; the finding by the FLORA European Project published in the journal Nature Biotechnology**

Researchers from the John Innes Centre in Norwich, Great Britain, in collaboration with other European centres participating to the FLORA project, have obtained genetically modified tomatoes rich in anthocyanins, a category antioxidants belonging to the class of flavonoids. These tomatoes, added to the diet of cancer-prone mice, showed a significant protective effect by extending the mice lifespan. The research has been published in the 26 October issue of Nature Biotechnology.



It is a remarkable step ahead in the study on antioxidants, particularly flavonoids, widely considered as a useful tool for preventing a large number of diseases, from cardiovascular disease to certain types of cancer. The diet followed by the majority of people living in the Western world does not appear to be sufficient to guarantee an adequate intake of these substances, present in many fruits and vegetables such as berries. That is why the FLORA project aims at understanding their mechanisms trying to find new ways to increase their consumption.

Researchers from the John Innes Centre, coordinated by Cathie Martin, tried to step on it by putting on the lab bench a naturally anthocyanins-free product as tomato and engineering it to enhance its flavonoid content. In this way researchers have obtained an ideal model to study the effect of anthocyanins.

In order to obtain fruit particularly rich in anthocyanins, that has conferred a peculiar purple colour to the tomatoes, the British team has used two genes from the snapdragon flower: Delila and Rosea1. "Our institute has a long standing interest in this plant that we use as a model to study flower development- says lead author Eugenio Butelli- The two genes we have isolated are responsible for flower pigmentation and, when introduced in other plants, turned out to be the perfect combination to produce anthocyanins, the same phytochemical found in blueberries. At a closer chemical analysis it comes out that our purple tomato has a very high antioxidant activity, almost tripled in comparison to the natural fruit thus it is very useful to study the effect of anthocyanins".

Subsequently, scientists have fed knockout mice lacking p53 gene, commonly known as the "genome guardian", with a powder obtained from purple tomatoes.

P53 is a key gene in the tumorigenesis process. Mice lacking p53 develop different types of tumours, especially lymphomas and die at a very young age.

Mice used in the experiment have been divided into three groups, fed three different diets: the first one has received a standard diet, while the second group was fed diet supplemented with 10% powder from freeze-dried red tomatoes and the last one with 10% powder from purple tomatoes. "We have not recorded significant differences between the first two groups- argues Marco Giorgio from the European Institute of Oncology who followed the experimental phase on mice-



But mice fed with purple tomatoes showed a significant increase of lifespan". The last group has reported an average lifespan of 182 days in comparison to the 142 recorded for mice fed standard diet.

However promising results appear to be, researchers prefer to be pretty cautious. "Actually- Giorgio continues- it is a pilot test, a preliminary study useful to validate the hypothesis of obtaining health benefits from diet supplementation with modified food. Although mice's lifespan has significantly increased once fed on purple tomatoes we still don't know how it works. It is not likely everything can be explained on antioxidants basis alone. Moreover, we have to consider that in this study we have not taken into account any possible toxicity so I shall say we're far from considering a human trial. Next step is to investigate the effect of purple tomatoes on different kinds of tumor models and define the mechanism of action".

Nevertheless, FLORA researchers do believe we may start to do something. "The study- says Cathie Martin, FLORA project coordinator- confirms the latest research trends arguing that we can obtain significant beneficial effects by simple changes in our daily diet. We are not talking of pills or supplements but only food. It is worthy of notice that recommendations by worldwide governments risk to be unaccepted. The 5-a-day program promoted by the American National Cancer Institute 20 years ago does not seem to be very incisive and not just because of the lack of time. Financial crisis is giving an hand to the failure of good intentions mainly due to the expensive costs of fruits and vegetables. Research has to do something, has to find new ways to face the challenge. A solution may rely on concentrating in few but selected products the largest part of nutrients we should intake during the whole day".

#### **The FLORA Project**

*Funded by the European Commission within the 6th framework program, the FLORA Project aims at gaining further evidence on the dynamics triggered by flavonoids, establishing a forefront in Europe for the study of association among these compounds and cardiovascular disease, myocardial infarction and tumours. FLORA researchers are involved in the field of flavonoids contained in different vegetables, such as corn, tomatoes and an experimental plant called Arabidopsis. Oranges too are other protagonists of this study. They are rich in flavonoids and phenolics by their own nature. FLORA's oranges have something more: the amount of antioxidant has been enriched in order to optimize their natural beneficial effects. Moreover, these fruits are additive free and have been cultivated in full respect of healthy parameters. There is no risk of unexpected surprises but just a measured increase in terms of nutrition. Promoting health through a balanced and correct diet, in respect for different food traditions of European Countries, is the mission of FLORA. Research Centres from different European Countries participate to the Project.*

### **Stress may make you itch**

Berlin, Germany — Current research suggests that stress may activate immune cells in your skin, resulting in inflammatory skin disease. The related report by Joachim et al., "Stress-induced Neurogenic Inflammation in Murine Skin Skews Dendritic Cells towards Maturation and Migration: Key role of ICAM-1/LFA-1 interactions," appears in the November issue of The American Journal of Pathology.

Skin provides the first level of defense to infection, serving not only as a physical barrier, but also as a site for white blood cells to attack invading bacteria and viruses. The immune cells in skin can over-react, however, resulting in inflammatory skin diseases such as atopic dermatitis and psoriasis.

Stress can trigger an outbreak in patients suffering from inflammatory skin conditions. This cross talk between stress perception, which involves the brain, and the skin is mediated through the "brain-skin connection". Yet, little is known about the means by which stress aggravates skin diseases.

Researchers led by Dr. Petra Arck of Charité, University of Medicine Berlin and McMaster University in Canada, hypothesized that stress could exacerbate skin disease by increasing the number of immune cells in the skin. To test this hypothesis, they exposed mice to sound stress. Dr. Arck's group found that this stress challenge resulted in higher numbers of mature white blood cells in the skin. Furthermore, blocking the function of two proteins that attract immune cells to the skin, LFA-1 and ICAM-1, prevented the stress-induced increase in white blood cells in the skin.

Taken together, these data suggest that stress activates immune cells, which in turn are central in initiating and perpetuating skin diseases. Fostered by the present observation, the goal of future studies in Dr. Arck's group is to prevent stress-triggered outbreaks of skin diseases by recognizing individuals at risk and identifying immune cells suitable to be targeted in therapeutic interventions.

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*Joachim RA, Handjiski B, Blois SM, Hagen E, Paus R, Arck PC: Stress-induced neurogenic inflammation in murine skin skews dendritic cells towards maturation and migration: key role of ICAM1/LFA-1 interactions. Am J Pathol 2008 173:1379-1388*