

## **Zinc supplements during pregnancy may counteract damage from early alcohol exposure**

Animal research has shown that binge drinking – even just once – during early pregnancy can cause numerous problems for the fetus, including early postnatal death. Fetal zinc deficiency may explain some of the birth defects and neurodevelopmental abnormalities associated with alcohol exposure. New rodent findings are the first to show that dietary zinc supplements throughout pregnancy can reduce some alcohol-related birth defects.

Results will be published in the April issue of *Alcoholism: Clinical & Experimental Research* and are currently available at Early View.

"Alcohol's damage to the fetus depends not only on the amount and duration of alcohol exposure, but also on the timing of the exposure relative to the development stage of the cells and tissues involved," said Peter Coyle, associate professor at the Hanson Institute in Adelaide, and corresponding author for the study. "Earlier work had shown that prenatal alcohol, as well as other toxins, can result in fetal zinc deficiency and teratogenicity by inducing the zinc-binding protein, metallothionein, in the mother's liver. Since then, our group has confirmed the importance of metallothionein in alcohol-mediated birth defects."

Coyle and his colleagues injected pregnant mice with either saline or a 25-percent solution of alcohol on gestational day (GD) eight; all mice received either a regular or zinc-supplemented diet from GD zero to 18. On GD 18, fetuses from all four groups – saline, saline plus zinc, alcohol, alcohol plus zinc – were assessed for external birth abnormalities. In addition, from birth to day 60, researchers examined the growth of survivors from all four groups.

"There were three key findings," said Coyle. "One, fetal abnormalities caused by acute alcohol exposure in early pregnancy can be prevented by dietary zinc supplementation. Two, dietary zinc supplementation throughout pregnancy can protect against post-natal death caused by acute alcohol exposure in early pregnancy. Three, dietary zinc supplementation increases the mother's blood zinc to overwhelm the transient drop in zinc caused by alcohol, which we believe prevents the fetal zinc deficiency and subsequent fetal damage."

Coyle added that the rodents' GD eight is the equivalent of weeks three to eight during a human pregnancy. "This encompasses a period when the mother is often unaware of her pregnancy and may not have changed her drinking habits," he said. "Moreover, up to 60 percent of pregnancies are unplanned. This latter point is of concern when noting that binge drinking is common in the community and more likely to occur in the first trimester than later." Importantly, Coyle emphasized, his team is not suggesting that it is safe to drink while taking zinc during pregnancy.

"We have not determined whether zinc protects against all of the possible negative outcomes from alcohol exposure in pregnancy," he said. "Nor would we recommend that makers of alcoholic beverages include zinc in their product so that women can drink while pregnant. Indeed, we take the conservative stand of a 'no alcohol policy' during pregnancy. What our studies do indicate is that dietary zinc supplementation could be as important as folic acid and applied as a simple prophylactic treatment in the human setting to prevent the effects of a range of insults in pregnancy."

While zinc supplementation is relatively common, and zinc tablets can easily be found in herbal shops, Coyle cautioned that zinc can also affect the absorption of other trace elements and cause anemia if taken in excess. "So one must be wary of taking zinc supplements without professional oversight, and this is particularly so in pregnancy," he said.

"Furthermore," he added, "although dietary zinc supplementation has been used in human pregnancy, we do not have any information regarding the dose that would be required to protect against damage from alcohol nor even the dosage that could be harmful to fetal development. Indeed, we have not tested our hypothesis in humans and so it would be unwise to extrapolate any of our findings to humans. We would predict that zinc supplementation would only be effective around the time of alcohol intake to prevent fetal zinc deficiency. Taking zinc supplements a day after alcohol consumption would probably be too late to prevent fetal damage. Obviously more research is needed."

## **Antibiotic-resistant gonorrhea increases from 2 percent to 28 percent**

The prevalence of quinolone-resistant gonorrhea has increased rapidly in Ontario – Canada's most populous province – from a rate of 2% in 2001 to 28% in 2006, found a study published in *CMAJ* <http://www.cmaj.ca/press/pg287.pdf>. Infections in heterosexual men appear to have contributed to the increased rate of resistance. Other studies have associated quinolone-resistant gonorrhea with men having sex with men, antibiotic use, over 35 years of age and travel to Asia.

"The magnitude of the rate of resistance to quinolone in Ontario is unusually high by any threshold reported in North America," state Dr. Susan Richardson from The Hospital for Sick Children (SickKids) and coauthors. "Given Ontario's large population and its status as a major economic centre and national transit hub, its epidemiology is likely to influence epidemiological trends in other provinces of Canada."

After several years of declining infection rates, *Neisseria gonorrhoeae* infections are on the rise in Canada and many other countries, with health ramifications as the disease can cause infertility and serious blood, joint and immune complications.

The study findings underscore the current recommendations in Canada not to use quinolones for treatment of *N. gonorrhoeae* infections. Ongoing testing for antibiotic resistance is necessary, although new testing methods are replacing methods that test for susceptibility. "The importance of using culture diagnostics for *N. gonorrhoeae* needs to be communicated to clinicians, laboratories and public health organizations," conclude the authors. In a related commentary <http://www.cmaj.ca/press/pg268.pdf>, Dr. John Tapsall from Prince of Wales Hospital in Sydney, Australia states "in developed countries, the spread of quinolone-resistant *N. gonorrhoeae* infection has followed a pattern in which different resistant subtypes are imported, sometimes over many years. The subtypes are eventually introduced into a country's sexual networks and then achieve sustained endemic transmission."

Appropriate antibiotic use is crucial for controlling drug-resistance in community-acquired pathogens. A sustained global approach is needed to reduce the rates of drug-resistant gonorrhea and to control the disease. All countries are at risk of the spread of even more resistant strains of this highly adaptable pathogen.

### **Vascular drug found to improve learning and memory in middle-aged rats** ***Drug has been well tolerated in humans for years***

WASHINGTON — A team of Arizona psychologists, geneticists and neuroscientists has reported that a safe and effective drug used to treat vascular problems in the brain has improved spatial learning and working memory in middle-aged rats. Although far from proving anything about human use of the drug, the finding supports the scientific quest for a substance that could treat progressive cognitive impairment, cushion the cognitive impact of normal aging, or even enhance learning and memory throughout the life span.

The finding appears in the February issue of *Behavioral Neuroscience*, which is published by the American Psychological Association. The drug in question, Fasudil, has been used for more than 10 years to treat vascular problems in the brain, often helping with recovery from stroke.

In this study, the researchers injected hydroxyfasudil, the active form of Fasudil, into middle-aged (17-18 months old) male rats daily starting four days before behavioral testing and continuing throughout testing. Injection made it easy to give the drug to rats, but people take it in pill form.

Rats were tested on the water radial-arm maze, which assessed how well they remembered which of the radiating arms had a reward, a sign of accurate spatial learning and working memory. Rats given a high dose (0.3750 mg per kg of weight) of hydroxyfasudil successfully remembered more items of information than those given a low dose (0.1875 mg per kg). Both dosed groups performed significantly better than control-group rats given saline solution. On this same test, the high-dose group showed the best learning (fewest total errors) and best working memory (measured two different ways).

For every test of learning, the scores of the low-dose group fell between the scores of the no-dose and high-dose groups, meaning that learning and memory boosts depended on the size of the dose.

The findings suggest that hydroxyfasudil may be involved in two crucial cognitive processes, learning and working memory, both involving the hippocampus. The mechanism is unclear, but hydroxyfasudil's parent drug, Fasudil, is known to protect the brain by dilating blood vessels when blood flow is curtailed. In the body, Fasudil breaks down into the more potent hydroxyfasudil molecule, which the authors hypothesize may alter memory by affecting the function of a gene called KIBRA. The authors recently demonstrated that KIBRA may play a role in memory in healthy young and late-middle-aged humans.

The authors wrote that their findings may have clinical relevance: "The collected findings and the relative safety of Fasudil support [its] potential ... as a cognitive enhancer in humans [who] have age- or neurodegenerative-related memory dysfunction."

Thus, said lead author Matthew Huentelman, PhD, "We have identified a drug that seems to benefit both the cardiovascular system, which it was originally designed to do, and the central nervous system, a new indication. We are actively exploring options for a clinical trial in the areas of cognitive impairment and dementia using the well-tolerated pro-drug Fasudil."

Co-author Heather Bimonte-Nelson, PhD, added that, "Fasudil shows great promise as a cognitive enhancer during aging. The effects in our aging animal model were robust, showing enhancements in both learning and two measures of memory. The possibility that these findings may translate to benefits to human brain health and function is very exciting."

Hydroxyfasudil inhibits the activity of Rho-kinase enzymes, which have been shown to inhibit Rac, a vital protein that supports key cellular functions. The authors speculated that blocking Rho-kinase enables Rac, in turn, to activate more of an enzyme called protein kinase C-zeta, which may in turn affect the KIBRA protein.

*The authors received financial support from the Evelyn F. McKnight Brain Research Foundation, the National Institute on Aging, the National Institute of Neurological Disorders and Stroke, and the state of Arizona. They maintain that they have no competing financial interests. Four of the authors hold stock in Sygnis Pharma AG, a German pharmaceutical company that owns the rights to develop this drug class as a potential memory enhancer. They stated that Sygnis was not directly involved in this study, did not fund any part of it, and did not influence the decision to study these drugs or the conclusion.*

*Article: "Peripheral Delivery of a ROCK Inhibitor Improves Learning and Working Memory," Matthew J. Huentelman, PhD, and Dietrich A. Stephan, PhD, Translational Genomics Research Institute, Phoenix, Arizona and Arizona Alzheimer's Consortium; Joshua Talboom, BS, Arizona State University; Jason J. Corneveaux, BS, David M. Reiman, undergraduate student, and Jill D. Gerber, BS, Translational Genomics Research Institute, Phoenix, Arizona; Carol A. Barnes, PhD, Arizona Alzheimer's Consortium and University of Arizona; Gene E. Alexander, PhD, Arizona Alzheimer's Consortium and University of Arizona; Eric M. Reiman, PhD, Arizona Alzheimer's Consortium and University of Arizona; Heather A. Bimonte-Nelson, PhD, Arizona Alzheimer's Consortium and Arizona State University, Tempe, Arizona; Behavioral Neuroscience, Vol. 123, No. 1. (Full text of the article is available from the APA Public Affairs Office and at <http://www.apa.org/journals/releases/bne1231218.pdf>)*

### **Insulin is a possible new treatment for Alzheimer's**

EVANSTON, Ill. --- A Northwestern University-led research team reports that insulin, by shielding memory-forming synapses from harm, may slow or prevent the damage and memory loss caused by toxic proteins in Alzheimer's disease.

The findings, which provide additional new evidence that Alzheimer's could be due to a novel third form of diabetes, will be published online the week of Feb. 2 by the Proceedings of the National Academy of Sciences (PNAS).

In a study of neurons taken from the hippocampus, one of the brain's crucial memory centers, the scientists treated cells with insulin and the insulin-sensitizing drug rosiglitazone, which has been used to treat type 2 diabetes. (Isolated hippocampal cells are used by scientists to study memory chemistry; the cells are susceptible to damage caused by ADDLs, toxic proteins that build up in persons with Alzheimer's disease.) The researchers discovered that damage to neurons exposed to ADDLs was blocked by insulin, which kept ADDLs from attaching to the cells. They also found that protection by low levels of insulin was enhanced by rosiglitazone. ADDLs (short for "amyloid beta-derived diffusible ligands") are known to attack memory-forming synapses. After ADDL binding, synapses lose their capacity to respond to incoming information, resulting in memory loss. The protective mechanism of insulin works through a series of steps by ultimately reducing the actual number of ADDL binding sites, which in turn results in a marked reduction of ADDL attachment to synapses, the researchers report.

"Therapeutics designed to increase insulin sensitivity in the brain could provide new avenues for treating Alzheimer's disease," said senior author William L. Klein, a professor of neurobiology and physiology in the Weinberg College of Arts and Sciences and a researcher in Northwestern's Cognitive Neurology and Alzheimer's Disease Center. "Sensitivity to insulin can decline with aging, which presents a novel risk factor for Alzheimer's disease. Our results demonstrate that bolstering insulin signaling can protect neurons from harm."

The amyloid beta oligomers, or ADDLs, form when snippets of a protein clump together in the brain. In Alzheimer's disease, when ADDLs bind to nearby neurons, they cause damage from free radicals and a loss of neuronal structures crucial to brain function, including insulin receptors. This damage ultimately results in memory loss and other Alzheimer's disease symptoms. The Alzheimer's drug Namenda has been shown to partially protect neurons against the effects of ADDLs.

"The discovery that anti-diabetic drugs shield synapses against ADDLs offers new hope for fighting memory loss in Alzheimer's disease," said lead author Fernanda G. De Felice, a former visiting scientist in Klein's lab and an associate professor at the Federal University of Rio de Janeiro, Brazil.

"Recognizing that Alzheimer's disease is a type of brain diabetes points the way to novel discoveries that may finally result in disease-modifying treatments for this devastating disease," adds Sergio T. Ferreira, another member of the research team and a professor of biochemistry in Rio de Janeiro.

In other recent and related work, Klein, De Felice and their colleagues showed that ADDLs bound to synapses remove insulin receptors from nerve cells, rendering those neurons insulin resistant.

The outcome of the molecular-level battle between ADDLs and insulin, which in the current PNAS study was found to remove ADDL receptors, may determine whether a person develops Alzheimer's disease. *In addition to Klein, De Felice and Ferreira, other authors of the PNAS paper, titled "Protection of Synapses Against Alzheimer's-linked Toxins: Insulin Signaling Prevents the Pathogenic Binding of A $\beta$  Oligomers," are Wei-Qin Zhao, a former visiting scientist at Northwestern, now with Merck & Co., Inc.; Pauline T. Velasco, Mary P. Lambert and Kirsten L. Viola, from Northwestern; and Marcelo N. N. Vieira, Theresa R. Bomfim and Helena Decker, from the Federal University of Rio de Janeiro, Brazil.*

## **Study identifies potential 'safe period' for hormone replacement use**

A new study makes important new findings on the role of hormone use on the risk of breast cancer, confirming that the use of estrogen plus progesterone increases the risk of both ductal and lobular breast cancer far more than estrogen-only; suggesting a two-year "safe" period for the use of estrogen and progesterone; and finding that the increased risk for ductal cancers observed in long-term past users of hormone replacement therapy drops off substantially two years after hormone use is stopped. The study appears in *CANCER*, a peer-reviewed journal of the American Cancer Society.

Previous studies have shown that hormone replacement therapy after menopause increases the risk of breast cancer and that use of a regimen that includes both estrogen and progesterone is more detrimental for the breast than the use of estrogen alone. But more data from large prospective studies are needed to fully characterize the impact of exogenous hormones on breast cancer incidence by type of hormone preparation and histology of the cancer.

To investigate the association in more detail, American Cancer Society epidemiologists led by Eugenia E. Calle, PhD, did a prospective study of 68,369 postmenopausal women who were cancer-free at baseline in 1992. They examined the use of estrogen-only and estrogen and progesterone in current and former users of varying duration, and the subsequent risk of developing invasive ductal and lobular carcinoma of the breast. They also looked at whether the risk for each type of breast cancer and each type of hormone regimen varied by body mass index (BMI), stage of disease at diagnosis, and estrogen receptor (ER) and progesterone receptor (PR) status. For the present study, the follow-up period ended on June 30, 2005.

They confirmed the findings from previous work that estrogen and progesterone increases the risk of both ductal and lobular breast cancer far more estrogen alone. They also found the risk associated with use of estrogen and progesterone increases significantly and substantially within three years of beginning hormone use. The data showed no increased risk for women who used estrogen and progesterone for less than two years, potentially identifying a "safe" period for estrogen and progesterone use.

The study also found no increased risk of breast cancer in women who had stopped using estrogen and progesterone two or more years ago, suggesting a window of two to three years for the risks of estrogen and progesterone both to become apparent after initial use and to diminish after cessation. Few estimates of risk within two to three years of initiation and cessation are available, so these findings need replication in other large studies.

The study found the use of estrogen and progesterone was associated with a doubling of risk of lobular cancer after three years of use, and a doubling of risk of ductal cancer with 10 years of use. Estrogen-only use was not associated with increased risk of ductal cancer, even after 20 years of use, but was associated with a 50 percent increase in risk of lobular cancer after 10 years of use.

*Article: "Postmenopausal hormone use and breast cancer associations differ by hormone regimen and histologic subtype." Eugenia E. Calle, PhD, Heather Spencer Feigelson, PhD, Janet S. Hildebrand, MPH, Lauren R. Teras, MPH, Michael J. Thun, MD, Carmen Rodriguez, MD, MPH CANCER; Published Online: January 20, 2008 (DOI: 10.1002/cncr.24101); Print Issue Date: March 1, 2009*

## **Plant Soybean Early to Increase Yield**

***New research shows that early planting does increase soybean yield, but can vary by year and cultivar choice.***

MADISON, WI, - Over the past decade, two-thirds of Indiana growers have shifted to planting their soybean crop earlier because they believe that earlier planting increases yield. Planting date is probably one of the most important yet least expensive management decisions that significantly affects soybean yield. Few scientists, however, have studied the effect of early-planting dates on soybean yield components and the impact of early planting on seed composition.

To answer this question, Andrew P. Robinson and colleagues at Purdue University conducted a 2-year (2006-2007) study at West Lafayette, IN. The research was supported by the Indiana Soybean Alliance and the Indiana Crop Improvement Association.

Three soybean cultivars were planted approximately every 2 weeks starting in late March and ending in early June. Detailed measurements of soybean yield components (pod number, seeds per pod, and seed mass), nodes, and reproductive nodes were counted by hand just before harvest. Oil and protein concentrations were determined by near-infrared reflectance spectroscopy.

A recent article in the January-February 2009 issue of *Agronomy Journal* gives detailed results from this study. This research was presented at the American Society of Agronomy annual meetings in October 2008 at

Houston, TX, and at the American Seed Trade Association, Corn, Sorghum, and Soybean annual meetings in December 2007 at Chicago, IL.

"The research found that yield was consistently the highest when planting from April to early May," comments Robinson.

Pods-per-square-meter were a good indicator of yield potential of early planted soybean, whereas seed mass was a good indicator of late-planted (late-May and early-June) soybean. Oil concentration was higher at early plantings and protein concentration was higher at late planting dates. As the temperature increased during R6 soybean growth stage (full seed) oil concentration increased and protein concentration decreased.

"Our research shows that early planting does increase yield, but can vary by year and cultivar choice. Our research also suggests that early planting may lead to increased oil concentration of Midwest soybean. However, early planting may not be for everyone," warns Robinson. "Further research is needed to quantify the impact early planting has on seed quality."

*The full article is available for no charge for 30 days following the date of this summary. View the abstract at <http://agron.scijournals.org/cgi/content/full/101/1/131>.*

## **Cementless Cup Device Developed for Total Hip Replacements Shows Durability after More than Twenty Years**

### ***Durability shown even with patients who had a previously failed hip replacement***

Chicago – When a first hip replacement fails, patients may be concerned that their options for a durable hip replacement are limited and that the prognosis is poor. However, a research study to be published in the February issue of the *Journal of Bone and Joint Surgery* suggests that this may not be the case.

Researchers from Rush University Medical Center examined their results using one of the first cementless metal cup designs and found that fixation of the implant to bone is extremely durable even twenty years after repeat or "revision" hip replacement. The implant utilized, the Harris-Galante-1 acetabular metal shell, which is designed to allow a patient's bone to grow into the implant, remained fixed in place in 95 percent of hip revision cases at a minimum follow-up of 20 years.

The implant and its bone in-growth surface were originally developed in conjunction with Dr. Jorge Galante, an orthopedic surgeon at Rush University Medical Center and one of the present study's investigators. The cup's porous surface allows bone and tissue to grow into the device to keep the hip implant in place. Earlier generation implants relied on the use of bone cement to secure the implant to the patient's pelvis and were associated with a higher rate of failure, particularly when used in patients who had previously had a hip implant that had failed.

"The study's results indicate that even the first generation of this device has excellent clinical results and durability," said Dr. Craig Della Valle, orthopedic surgeon at Rush and study investigator. "Even after 20 years, there is low rate of failure in terms of fixation."

Researchers previously reported the results of the use of the Harris-Galante-1 cementless acetabular shell for total hip revision procedures in 138 hips at a minimum of three, seven, and fifteen years postoperatively. The current report presents the long-term outcomes of this group at a follow-up of 20 years.

Of the original cohort of 138 hips, researchers were able to follow 73 patients who were still living (77 hips) for 20 years or more. Of the 77 hips, 37 had both clinical and radiographic evaluation, 20 had a clinical evaluation via telephone questionnaire and 21 underwent a repeat revision of the acetabular metal shell.

Twenty of the 21 cementless cups were found to be well fixed at the time of repeat revision and only one had become loose. During the entire study period, four cups were identified radiographically as being loose. For the entire cohort of 138 hips, the 20-year survivorship of the acetabular component was 95 percent.

While the long-term fixation of the device performed very well, the study did find an increased rate of repeat surgery for wear-related complications compared to the 15-year report. Ten patients, or 18 percent, had a complication related to wear of the bearing surface as opposed to 3 percent at 15 years.

"Although we have seen more complications related to wear as we have continued to follow these patients, our studies have taught us valuable lessons regarding failure mechanisms and how to avoid them," said Della Valle.

Despite the increasing prevalence of wear-related problems, the main modes of failure were infection and recurrent dislocations. The study authors recommend the use of larger diameter femoral heads and more wear-resistant bearings to decrease the risks of these complications.

"We can continue to make vast improvements in the quality of bearing and stability in the next generation of devices used in total hip replacements with the information we have gathered from this study," said Galante. "More and more patients are living longer and we must continue to further develop sustainable devices that will give patients a better quality of life."

## **Small male chimps use politics, rather than aggression, to lead the pack, U of Minnesota study says**

With most mammals, the biggest and most aggressive male claims the alpha male role and gets his choice of food and females. But a new study from the University of Minnesota suggests that at least among chimpanzees, smaller, more mild-mannered males can also use political behavior to secure the top position.

The finding was gleaned from 10 years of observing dominant male chimpanzees in Gombe National Park, Tanzania, looking at behaviors they used to compete for alpha male status relative to their size. Analysis showed that larger males relied more on physical attacks to dominate while smaller, gentler males groomed other chimpanzees, both male and female, to gain broad support.

The study focused on three alpha males who reigned between 1989 and 2003. Frodo, one of the largest and most aggressive male chimpanzees ever observed at Gombe, weighed 51.2 kg (112.6 lbs.) at his peak. He relied on his size and aggression to rule. While he allowed other chimpanzees to groom him, he seldom returned the favor. At the other end of the spectrum, Wilkie, who weighed only 37 kg (81.4 lbs.), obsessively groomed both male and female chimpanzees to maintain his top position. And Freud, who weighed 44.8 kg (98.6 lbs.), used a combination of the two strategies. (The average male chimp in Gombe weighs about 39 kg (85.8 lbs.).)

The findings are reported in the February issue of the *American Journal of Primatology*. While it's widely known that grooming plays an important role in chimpanzee social interaction, this study is the first to show that it can be a strategy for achieving dominance.

Mark Foster, who was an undergraduate pursuing a bachelor of arts degree in anthropology and a B.F.A. in acting when the research was conducted, was the study's lead author of the study. As a recipient of a Katherine E. Sullivan Fellowship he later spent six months in Tanzania and Gombe and then became an educational assistant at the Lincoln Park Zoo in Chicago.

"Mark showed extraordinary creativity and tenacity in pulling together this study while still an undergraduate and then seeing it through to publication," said Anne Pusey, who was senior author. Pusey is director of the Jane Goodall Institute's Center for Primate Studies at the University of Minnesota and a University McKnight Distinguished Professor in the College of Biological Sciences' department of ecology, evolution and behavior (EEB).

Other collaborators included EEB graduate students Ian Gilby, who guided Foster in the initial outline of the question and in data extraction; Carson Murray, who guided data analysis; and Emily Wroblewski, who analyzed data on male dominance hierarchies. Statistics graduate student Alicia Johnson of the U of M Statistics Clinic guided the statistical analysis. Gilby is now a post-doctoral fellow at Harvard, and Murray a post-doctoral fellow at Lincoln Park Zoo.

"We were aware that Frodo was a bully and a stingy groomer, but we did not know how closely grooming patterns would correlate with body size," Pusey said. "We plan to study more alpha males to determine if grooming is a common strategy that small-bodied males use to placate rivals or cultivate cooperative alliances."

### **New Vaccine Developed for Preventing "Uncommon Cold" Virus**

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FAIRFAX, Va. - Common colds typically cause a week of sneezing, aches and pains and then fade away leaving only a sore nose and a few used sick days behind. But what if that cold turned out to be something more?

Human adenovirus type-3 is known as the "uncommon cold" because the infection's symptoms—runny nose, sore throat, cough and fever—are eerily similar to those of the common cold which is caused by the rhinovirus. The difference is that, unlike the common cold, the symptoms of the uncommon cold are typically much more severe and can even be fatal.

Adenovirus-3 thrives in nations with dense urban populations and has recently become prevalent in southern China and neighboring countries. It may also emerge in less likely locales with dense populations, such as schools, health care facilities and military training bases in the U.S.

Determined to stamp out this devastating infection, researchers from George Mason University, the University of Hong Kong, Guangzhou Children's Hospital, the South China Institute of Technology and the Graduate School of Chinese Academy of Sciences have developed a DNA-based vaccine that has effectively protected mice from the infection. Their findings will appear in the February 18, 2009 print edition of the journal *Vaccine* and are currently available online.

"Further study is required, but we hope that in the future, this simple, stable and inexpensive vaccine can be mass-produced and made available to susceptible populations," says Donald Seto, associate professor in George Mason University's Department of Bioinformatics and Computational Biology, the only U.S.-based researcher involved in the study. "Affordability is a key factor since these regions are generally economically depressed."

According to the Centers for Disease Control and Prevention (CDC), the human adenovirus was first seen in the 1950s and is associated with a wide spectrum of illnesses including conjunctivitis, upper respiratory infections, pneumonia and gastrointestinal disease. More than 50 unique serotypes of the virus have been identified, with even more expected to be isolated.

Adenovirus outbreaks are difficult to control because the virus can live for weeks on environmental surfaces and spreads quickly through direct contact, aerosol and contaminated drinking water.

Although the disease is relatively rare in the U.S., CDC records indicate that it has made several appearances here with devastating results. In 2000, four children died during an outbreak of adenovirus type-7 that occurred at a long-term care facility in Iowa, and nine patients died when adenovirus type-14 appeared as epidemics in Oregon, Texas and Washington in 2007.

Seto hopes that this new vaccine will serve as a model that allows his team to target the remaining strains of the virus. “The immediate impact is the production and distribution of a low-cost, stable vaccine for adenovirus-3,” says Seto. “The outstanding question is, if all of the strains are so similar, why are they restricted to certain tissues, like only the eyes or the respiratory tract? That’s what we’ll try to figure out next.” *The paper was co-authored by Qiwei Zhang, Xiaobo Su, Bo-jian Zheng, Xingui Tian, Huiying Sheng, Haitao Li, Youshao Wang and Rong Zhou. The study was funded by the National Natural Science Foundation of China.*

### **Slow down -- those lines on the road are longer than you think**

Columbus, Ohio -- Take a guess -- how long are the dashed lines that are painted down the middle of a road?

If you’re like most people, you answered, “Two feet.”

The real answer is 10 feet. That’s the federal guideline for every street, highway, and rural road in the United States, where dashed lines separate traffic lanes or indicate where passing is allowed.

A new study has found that people grossly underestimate the length of these lines -- a finding which implies that we’re all misjudging distances as we drive, and are driving too fast as a result.

Dennis Shaffer, assistant professor of psychology at Ohio State University’s Mansfield campus, led the study, which appeared in the journal *Perception & Psychophysics*. Shaffer and his colleagues tested more than 400 college students in three experiments. When asked to guess the length of the lines from memory, most answered two feet. Even when the students were standing some distance away from actual 10-foot lines or riding by them in a car, they judged the size to be the same: two feet. “We were surprised, first, that people’s estimates were so far off, and second, that there was so little variability,” Shaffer said.

The finding holds implications for traffic safety. Each dashed line measures 10 feet, and the empty spaces in-between measure 30 feet. So every time a car passes a new dashed line, the car has traveled 40 feet. But in this study, people consistently judged the lines and the empty spaces to be the same size, claiming that both were two feet. “This means that to most people, 40 feet looks like a lot less than 40 feet when they’re on the road,” Shaffer said. “People cover more ground than they think in a given period of time, so they are probably underestimating their speed.”

He acknowledges that the study will come as no surprise to transportation engineers, some of whom his team consulted with during the study. But this is the first study to quantify Americans’ misperceptions of the lines.

Shaffer began this research when he was a graduate student at Kent State University in 1995, and continued it while he was on the faculty of Arizona State University’s West Campus, and now at Ohio State. At each university, he and his colleagues measured lines on a variety of roads in the area.

Over those years, the federal guideline for line size has shrunk from 15 feet to 10 feet. Wherever the researchers went, they found all lines to be close to the federal guidelines of the time. In Arizona in 2000, for instance, some lines were 16 feet long instead of the expected 15.

But even back then -- when the federal guideline was 15 feet -- people still thought of lines as measuring only two feet. “It was ridiculous,” Shaffer said. “We talked to different people in different states, over different years, and whether the lines were 15 feet or 10 feet, people still estimated them to be two feet.”

One possible explanation: as we drive, we look out far ahead the car for safety reasons, so the only lines we really see are faraway lines that look small.

Even though lines appear to expand as a car passes by, drivers can’t safely notice that effect. Rather, the first line we can comfortably look at while driving safely is some 120 feet ahead -- the fourth line ahead on the road. So perhaps we think that all lines are as small in reality as that one faraway line appears to be.

Some researchers have proposed the idea of “size constancy” to explain our perceptions -- meaning that we see an object as being the same size, no matter how close or far away it is, Shaffer said.

“That seems to be the case for lines on the road, because even if you know how long they are, they still look two feet,” he added. “To have a correct perception of the size of an object, you have to be familiar with the

object in advance. And that's the clincher. Very few people are familiar with the size of a line on the road in advance."

In the first experiment, researchers gave participants a written test in which they were asked how long they believed the lines and the spaces in-between to be. In the second experiment, the researchers took a piece of paper that was the exact size and shape of a dashed line and taped it to the ground. Participants stood either 60 or 120 feet from the line, and looked at it at an angle close to their line of sight, as they would see it if they were driving down a road. In the third experiment, participants sat in the front or rear passenger seat of a car, and were asked to study the lines and spaces while a researcher drove down an actual road at either 25 or 60 miles per hour.

As to why everyone's estimates were consistent in every experiment, Shaffer suspects that the answer has something to do with how our brains perceive geometry. Engineers design roads, buildings, and public spaces using Euclidian geometry -- the system of lines and angles first described by the ancient Greek mathematician Euclid. But this study and previous ones suggest that our brains perceive objects in a non-Euclidian way.

In the future, Shaffer will examine how people perceive the size of lines that are oriented at different angles -- as if seen by a driver approaching a bend in a road -- and how our perceptions affect our ability to judge the steepness of hills.

His coauthors on the paper included Andrew Maynor, formerly an undergraduate psychology student at Ohio State who is now a graduate student in labor and human resources in the Fisher College of Business; and Windy Roy, formerly an undergraduate psychology student at Arizona State University's West Campus.

### **Inflammation in Colon May Get Doused Before Fueling Cancer Development**

***Repeated inflammation that leads to colon cancer may have met its match. A tiny molecule, quercetin, found in most plant-based foods douses the flames before damaging lesions can form in the colon. [Texas AgriLife Research scientist Dr. Nancy Turner describes her study.](#)***

A tiny molecule found in most plant-based foods douses the flames before damaging lesions can form in the colon, according to a study by Texas AgriLife Research scientist Dr. Nancy Turner.

Even better, the compound can be obtained easily by eating vegetables and fruit rather than by taking expensive prescriptions or supplements, Turner said.

The molecule is quercetin. Tiny but potent, quercetin gets into the body through onions, peppers, tomatoes and most other common produce but also in "fun things like wine," she said. "Just about any plant-based food in the human diet has some level of quercetin."

Previous studies showed quercetin was effective in reducing the rate of colon cancer in laboratory tests, but Turner's latest research, published in the Journal of Nutrition, shows how the compound works. That means researchers may now begin to understand how quercetin could help other inflammatory bowel diseases such as Crohn's and celiac disease.

"The nice thing is that albeit high relative to what you see in the American diet, the level used in this study is actually similar to what can be achieved in diets around the world such as in, say, the Mediterranean-style diets," she said. "So it's not an unachievable goal for us good ol' Americans if we do the right thing with our food consumption."

For this study, Turner's team examined the response of quercetin-supplement diets in lab rats -- some in the early stages of colon cancer formation and others without cancer.

"Early lesions in a colon are some of the first true changes in the colon that can be observed visually," she said. "This is not just something you see in our animal model. You see it in human patients as well."

Called "aberrant crypts," they are thought to be a marker or predictor of tumor formation. Quercetin is known to reduce the number of these crypts, she noted, "But we wanted to know how it might be protecting." Cancer is often characterized as an uncontrolled growth in our bodies, but scientists now say that a natural process of cell death, or "apoptosis," is also critically important in cancer, Turner said. That is, a healthy body should have an equilibrium between new cells and cells that have done their job and are ready to be sloughed off.

"We found that we were deriving benefit from both of those," Turner said of the quercetin diet study. "We were able to decrease the number of cells that were proliferating in the colon. And we were able to increase the number of cells that were undergoing apoptosis. So the net effect of that is, we were able to maintain almost a normal number of cells."

Turner's team then decided to examine relatively new findings -- that inflammation is one of the biggest contributors of the development of colon cancer.

They targeted two enzymes -- known to researchers as Cox-1 and Cox-2. The first is a routine protein that the body expresses all the time, she said. But the second Cox has implications in a lot of diseases.



"Cox-2 is an inducible protein that is expressed in the body when there is some kind of external stimulus to a cell. We think of high levels of Cox-2 as being a bad thing."

One of those bad things is colon cancer. Not only is Cox-2 present in that disease, but recent research showed that before Cox-2 levels rose in colon cancer, the Cox-1 levels first became elevated. Cox-1, therefore, has some sort of control over whether Cox-2 gets expressed, she explained.

"We did see that both groups – both the control groups and the carcinogen-injected groups that were consuming quercetin in their diets – had lower levels of both Cox-1 and Cox-2," Turner said. "So that would tend to suggest that there may be opportunity for quercetin to suppress tumor development."

She said that additional research is needed on this portion of the work to better understand the connections. But she advised people to go ahead and eat plenty of fruits and vegetables.

"Overall, one of the best recommendations we've all heard from the day we were children is 'an apple a day keeps the doctor away.' The only addition is, don't peel your apple," she said. Compounds such as quercetin in plants are initially there to protect the plant against pests, UV sun rays and other problems, Turner said. "So these compounds are located where the plant most needs them, which is typically on the outside – in the peel. Try your best to eat the whole food where ever possible, so that you can get the most from these beneficial compounds."

She noted that in addition to colon cancer, quercetin has shown positive impacts in warding off other chronic ailments such as cardiovascular disease.

*Turner's research was funded by the U.S. Department of Agriculture and the Vegetable and Fruit Improvement Center at Texas A&M University.*

### **Hopkins Transplant Surgeons Remove Healthy Kidney Through Donor's Vagina - Minimally invasive organ removal could increase donations, surgeons say**

In what is believed to be a first-ever procedure, surgeons at Johns Hopkins have successfully removed a healthy donor kidney through a small incision in the back of the donor's vagina.

"The kidney was successfully removed and transplanted into the donor's niece, and both patients are doing fine," says Robert Montgomery, M.D., Ph.D., chief of the transplant division at Johns Hopkins University School of Medicine who led the team that performed the historic operation.

The transvaginal donor kidney extraction, performed Jan. 29 on a 48-year-old woman from Lexington Park, Md., eliminated the need for a 5-to-6-inch abdominal incision and left only three pea-size scars on her abdomen, one of which is hidden in her navel.

The novel surgery was performed by Mohamad E. Allaf, M.D., assistant professor in the departments of Urology and Biomedical Engineering and director of minimally invasive and robotic surgery. Allaf has performed a previous transvaginal nephrectomy on a diseased kidney, but this was the first time he has operated on a kidney donor. "In contrast to removing diseased kidneys, this procedure has to deliver a perfect kidney since it will be used by the recipient," says Allaf.

Transvaginal kidney removals have been done previously to remove cancerous or nonfunctioning kidneys that endanger a patient's health, but not for healthy kidney donation. Because transplant donor nephrectomies are the most common kidney removal surgery — 6,000 a year just in the United States — this approach could have a tremendous impact on people's willingness to donate by offering more surgical options," says Montgomery.

"Since the first laparoscopic donor nephrectomy was performed at Johns Hopkins in 1995, surgeons have been troubled by the need to make a relatively large incision in the patient's abdomen after completing the nephrectomy to extract the donor kidney. "That incision is thought to significantly add to the patient's pain, hospitalization and convalescence," says Montgomery. "Removing the kidney through a natural opening should hasten the patient's recovery and provide a better cosmetic result."

Both laparoscopies and transvaginal operations are enabled by wandlike cameras and tools inserted through small incisions. In the transvaginal nephrectomy, two wandlike tools pass through small incisions in the abdomen and a third flexible tool housing a camera is placed in the navel.

Video images displayed on monitors guide surgeons' movements. Once the kidney is cut from its attachments to the abdominal wall and arteries and veins are stapled shut, surgeons place the kidney in a plastic bag inserted through an incision in the vaginal wall and pull it out through the vaginal opening with a string attached to the bag.

Montgomery says the surgery took about three and a half hours, roughly the same as a traditional laparoscopic procedure.

The Jan. 29 operation is one of a family of new surgical procedures called natural orifice transluminal endoscopic surgeries (NOTES) that use a natural body opening to remove organs and tissue, according to

Anthony Kalloo, M.D., the director of the Division of Gastroenterology at Johns Hopkins University School of Medicine and the pioneer of NOTES. The most common openings used are the mouth, anus and vagina.

Since 2004, successful NOTES in humans have removed diseased gallbladders and appendixes through the mouth, and gallbladders, kidneys and appendixes through the vagina.

Recently, Kalloo says, some medical experts have called for more studies to compare the safety and effectiveness of NOTES against traditional laparoscopies, which also leave very small scars, have been in use for many years, and are proven to be safer and less painful for patients than older “open” abdominal procedures. He supports more studies.

But, he adds, “natural orifice transluminal endoscopic surgery is the final frontier to explore in making surgery scarless, less painful and for obese patients, much safer.” An organ donor, in particular, is most deserving of a scar-free, minimally invasive and pain-free procedure.”

*Additional surgeons from Johns Hopkins University School of Medicine who participated in the procedure were Andy Singer, M.D., Ph.D., assistant professor in the Division of Transplant Surgery; and Wen Shen, M.D., M.P.H., assistant professor in the Department of Gynecology and Obstetrics.*

### *A kind of 21<sup>st</sup>-Century kappa ...*

## **Cell-Building Discovery Could Reduce Need for Some Animal Research**

***Brown University biomedical engineers, using a 3-D Petri dish they invented, have successfully built complex-shaped microtissues by assembling small building blocks of living cell clusters. The finding, to be published in the March 1 edition of Biotechnology and Bioengineering, helps advance the field of tissue engineering and could reduce the need for some animal research.***

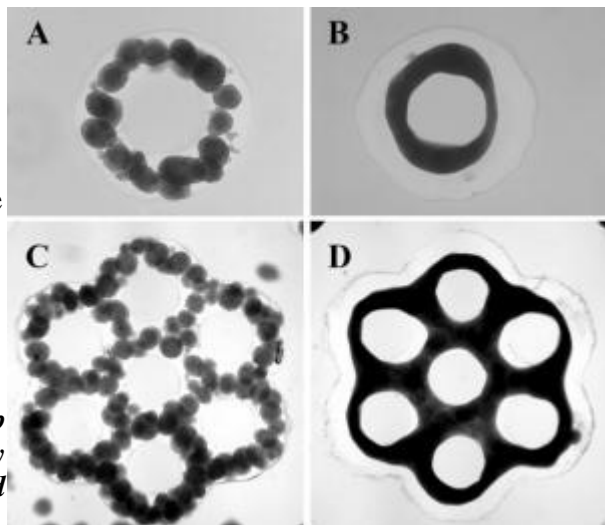
PROVIDENCE, R.I. [Brown University] — Brown University biomedical engineers can now grow and assemble living microtissues into complex three-dimensional structures in a way that will advance the field of tissue engineering and may eventually reduce the need for certain kinds of animal research.

The team, led by Brown professor Jeffrey Morgan, successfully used clusters of cells grown in a 3-D Petri dish also invented by the group, in order to build microtissues of more complex shapes.

Such a finding, detailed in the March 1 issue of *Biotechnology and Bioengineering* and posted at the end of January on the journal’s Web site, has enormous implications for basic cell biology, drug discovery and tissue research, Morgan said.

Because the tissues Morgan’s team created in the lab are more like natural tissue, they can be constructed to have complex lace-like patterns similar to a vasculature, the arrangement of blood vessels in the body or in an organ. Morgan said that added complexity could eventually reduce the need to use animals in certain kinds of research. The National Science Foundation and the International Foundation for Ethical Research funded the study, with the latter group’s mission focused in part on reducing the use of animals in research.

***Microtissues and molds*** Researchers are now able to develop complex microtissues (B,D) that take on the shape of molds they have designed into a 3-D Petri dish (A,C). That technique could reduce the need for certain kinds of animal-based research.



Morgan Lab/Brown University

“There is a need for ... tissue models that more closely mimic natural tissue already inside the body in terms of function and architecture,” said Morgan, a Brown professor of medical science and engineering. “This shows we can control the size, shape and position of cells within these 3-D structures.”

But Morgan said the finding also makes an important contribution to the field of tissue engineering and regenerative medicine. “We think this is one step toward using building blocks to build complex-shaped tissues that might one day be transplanted,” he said.

The new finding builds on earlier work by Morgan and a team of Brown students, which appeared in September 2007 in the journal *Tissue Engineering*. The earlier study highlighted the invention of a 3-D Petri dish about the size of a peanut-butter cup and made of agarose, a complex carbohydrate derived from seaweed with the consistency of Jell-O. Morgan and students in his lab developed the dish, creating a product where cells do not stick to the surface. Instead, the cells self-assemble naturally and form “microtissues.”

For the new research, Morgan, with students including Adam Rago and Dylan Dean, made 3-D microtissues in one 3-D Petri dish, harvested these living building blocks and then added them to more complex 3-D molds shaped either like a honeycomb, with holes, or a donut with a hole in the middle.

Those skin cells fused with liver cells in the more complex molds and formed even larger microstructures. Researchers found that the molds helped control the shape of the final microtissue.

They also found that they could control the rate of fusion of the cells by aging them for a longer or shorter time before they were harvested. The longer the wait, Morgan found, the slower the process.

Rago has since graduated from Brown, and Dean, an M.D.-Ph.D. student, has moved on from the Morgan lab to pursue his surgical rotations.

## **Gastric 'condoms' could help obese avoid surgery**

\* 02 February 2009 by **Peter Aldhous**

GASTRIC surgery is a last resort for people who are dangerously obese. But there may soon be a gentler option in the shape of a removable device inserted into the gut through the mouth.

The EndoBarrier, developed by GI Dynamics of Lexington, Massachusetts, is an impermeable sleeve that lines the first 60 centimetres of the small intestine. In animal experiments and preliminary human trials, it reduces weight and rapidly brings type II diabetes under control.

Given the rising tide of obesity across the developed world, new treatments are a matter of priority. In the US alone, more than 15 million adults meet the criteria for gastric surgery because they have a body mass index of more than 40, or a BMI of 35 plus a complication such as diabetes.

While the operations do cause dramatic and sustained weight loss, their high cost and concerns about the risk of dying on the operating table mean only a fraction of those who might benefit go on to have the surgery. According to the American Society for Metabolic and Bariatric Surgery, around 220,000 people in the US had gastric surgery for weight loss in 2008.

GI Dynamics is not the only company working on alternatives (see "Wired for weight loss"), but its approach is appealing for its simplicity and low cost. The device, enclosed in a capsule, is inserted via the mouth using an endoscope. Once in place below the base of the stomach, the capsule releases a small ball that with the help of a catheter pulls a flexible sleeve made of the slippery polymer PTFE through the intestine. The ball is jettisoned and the sleeve fixed in place by releasing a spiked attachment made from the shape-memory metal alloy nitinol (see diagram).



*Video: [Technology to tackle obesity](#)*

The entire process takes less than half an hour, and the EndoBarrier can also be removed in less than 10 minutes by tugging on a drawstring to collapse the attachment device and pull out the spikes. The EndoBarrier is then pulled back out through the mouth.

At the Massachusetts General Hospital in Boston, a team led by gastroenterologist Lee Kaplan has shown that a miniature version of the sleeve causes weight loss in rats equivalent to a popular form of gastric surgery in humans, where food intake is restricted by an adjustable band placed around the top of the stomach (Obesity, vol 12, p 2585).

"We aren't doing anything to the stomach, so the patient can still eat normally," says Stuart Randle, president of GI Dynamics, who adds that some patients given gastric bands find ways to fulfil their cravings for more calories. "They can do a lot of creative things - basically putting food into blenders," he says.

Kaplan's team also found that the device caused a rapid reversal of type II diabetes, even before the weight loss kicked in, thought to be the result of changes in neural and hormonal signals sent from the gut. This also happens in patients given a gastric bypass, in which the gut is replumbed to miss out a large part of the stomach and part of the small intestine.

The weight loss triggered by the device is larger than can be explained simply through reduced absorption of nutrients, Kaplan adds. So that, too, seems to be driven mainly by changes to gut physiology.

Around 150 people have tested the device, with similar effects to those seen in rats. Randle says the total cost of the EndoBarrier, including installation and removal, will be around \$7500. This compares to \$15,000 or more for inserting a gastric band, or at least \$20,000 for a gastric bypass.

More extensive trials will be needed to ensure the device is effective and can safely be left in the gut for long periods, says David Flum, who studies the outcomes of gastric surgery at the University of Washington in Seattle. "We don't really know what the implications will be."

But if the studies prove successful, many more obese people could have access to potentially life-enhancing weight loss treatment.

## **Wired for weight loss**

BEFORE doctors knew peptic ulcers were caused by a bacterial infection that can be treated with antibiotics, one approach was to cut the vagus nerves to reduce the release of stomach acid. This had an interesting side effect: many patients lost weight.

Now EnteroMedics of St Paul, Minnesota, aims to treat obesity using an electronic device that blocks vagus nerve signals to the gut. This seems to suppress appetite, inhibit the expansion and emptying of the stomach, and reduce the secretion of digestive enzymes. "It allows patients not to feel as hungry and to feel fuller much sooner," says EnteroMedics president Mark Knudson.

The vagus nerves descend from the brainstem, branching out to organs including the heart and the larynx, as well as the gut. The EnteroMedic device blocks signals to the gut by electrically stimulating the nerves just below the diaphragm at a frequency of 5 kilohertz. The electrodes are connected to a controller implanted beneath the skin above the ribs. Radio signals both program the device and recharge its battery.

When the vagus nerves are cut the body tends to adapt so in time shed weight can pile back on. To prevent this, EnteroMedics' device blocks signals for 5 minutes, shuts down for the next 5 minutes, and repeats this cycle throughout the day. It is also switched off at night.

The cost of device, now being tested in some 300 obese patients, will fall somewhere between a gastric-band operation and the costlier, more radical gastric bypass.

## **Random checks 'as effective' as terrorist profiling**

\* 22:00 02 February 2009 by Peter Aldhous

"Flying while Muslim" is the new "driving while black", according to air travellers who believe they are being targeted for extra security measures on the basis of racial and religious profiling.

Not only is profiling discriminatory, but it is also inefficient, according to a new analysis by William Press of the University of Texas at Austin. His argument applies not only to crude racial profiling, but also to profiles that flag up risky individuals on the basis of how they bought their tickets, whether they have checked luggage, whether they have purchased one-way flights, and so on.

Press has modelled situations in which members of a profiled group are, for example, 100 times more likely to be a terrorist than a typical traveller. You might think that the best approach would be to make it 100 times more likely that these people are selected for extra security checks. But in fact, random screening turns out to be just as effective.

The problem is that too much time is spent repeatedly screening members of the profiled group who are not actually terrorists, Press explains. For the same reason, a strategy in which members of the profiled group are always pulled aside performs more poorly than random screening, diverting resources from members of the "low risk" majority who may still be terrorists.

### **Waste of resources?**

A better approach, Press says, would be to take the square root of the extra risk posed by the profiled group, and use that number to define the likelihood that someone from the group will be pulled out of line. Under this scheme, members of a profiled group who are 100 more likely to be a terrorist than the typical traveller would be 10 times more likely to be given secondary checks.

Given the rarity of actual terrorists, however, this still may not be much better than random screening. "We probably shouldn't be doing profiling at all," Press suggests, once you weigh up the debatable benefits against concerns about discrimination.

In any case, quantifying the risk posed by a profiled group may be extremely difficult. "Fortunately, terrorists are few and far between," says Barry Steinhardt of the American Civil Liberties Union, which opposes the profiling of air travellers by whatever means. "We don't have enough information to create that profile."

The US Transportation Security Administration (TSA) denies that travellers are targeted for screening on racial or religious grounds. It has also abandoned attempts to create algorithms that would create non-racial profiles to identify particular travellers as posing a heightened risk.

Instead, the TSA is trying to improve the existing system, which always targets for extra screening people whose names have been placed on a "selectee" watch list.

*Journal reference: Proceedings of the National Academy of Sciences (DOI: 10.1073/pnas.0813202106)*

## **Google Earth provides dizzying 3D views of Mars**

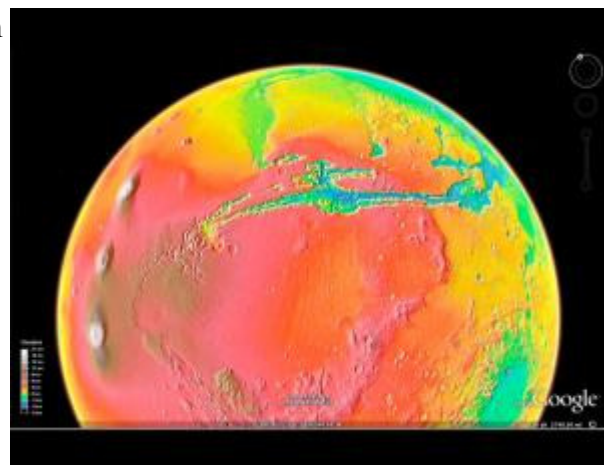
\* 01:22 03 February 2009 by Rachel Courtland

Mars enthusiasts can fly from the towering peak of Olympus Mons to Mars Pathfinder's peaceful resting place in an add-on to the latest version of the desktop application Google Earth, which was released on Monday.

The new Mars map amasses some 1000 gigabytes of data from a range of Mars probes, including NASA's Viking orbiters, Europe's Mars Express orbiter, and six landers, such as NASA's twin rovers, to create a three-dimensional view of the planet at a wide range of scales.

"What we've done is bring all that information into one single, easy-to-use platform," says Matthew Hancher of NASA's Ames Research Center in Moffett Field, California. "Everything that's ever gone to Mars has been put together to give us this unified view of the planet."

The new tool is accessible enough to appeal to a wide audience, but Hancher hopes the tool will also help researchers by allowing them to determine what data is available - such as infrared images and mineral maps made by orbital spectrometers - for particular regions of interest.



*Images from past and current Mars probes are combined to create a global, three-dimensional exploration tool in the new version of Google Earth (Illustration: Google)*

### **Interactive software**

The software is intended to be interactive, allowing users to draw lines, add text, embed videos, and add images. Researchers may also [add new content](#), which must be encoded in a language called KML in order to be properly overlaid on the globe. So far adding new data to the Mars layer is not automated, and only a few hundred images from the HiRISE camera aboard NASA's Mars Reconnaissance Orbiter - the most powerful camera ever sent to another planet - have been added, Hancher says.

The new software is an outgrowth of Google Mars, an online tool that allows users to [view two-dimensional maps of the Red Planet](#), pieced together from images taken by Mars Global Surveyor and Mars Odyssey. Read more about how to use the new Mars features in the [Google Earth Blog](#).

### **Green tea may negate the effects of a common cancer therapy**

WASHINGTON – Green tea products have become regarded as a valuable health supplement, as studies have shown evidence of its benefit against a variety of diseases, including cancer. However, a new study suggests that some components of green tea may counteract the anticancer effects of one cancer therapy, bortezomib (Velcade®), and may be contraindicated for patients taking this medicine to ensure its maximum therapeutic benefit. This study is being prepublished online today in *Blood*, the official journal of the American Society of Hematology.

Because of its increasing popularity and availability to the public in many formulations, green tea has been increasingly studied to understand its effect on cancer, heart disease, and other conditions. In animal studies, an antioxidant compound in green tea called the EGCG polyphenol (epigallocatechin gallate) has been shown to be a potent anticancer agent, with effects demonstrated against leukemia, as well as lung, prostate, colon, and breast cancer. Among other properties, EGCG binds to a common protein in tumors called GRP78 (which is responsible for preventing cell death) and inhibits its function, thereby assisting in the death of tumor cells.

"We know that cancer patients look to green tea extracts among other natural supplements to complement their therapeutic regimens. We wanted to better understand how the compounds in green tea interact with a cytotoxic chemical therapy and how that may affect patient outcomes," said Axel Schönthal, PhD, of the University of Southern California Keck School of Medicine and senior study author.

In this study, researchers evaluated whether the combination of green tea and bortezomib would improve outcomes against multiple myeloma, a blood cancer, and glioblastoma, a malignant brain tumor. Bortezomib, an anticancer therapy approved to treat multiple myeloma and mantle cell lymphoma, normally fights disease by inhibiting proteasomes and inducing tumor cell death. However, in both in vitro and in vivo mouse experiments, the team was surprised to find that the EGCG compound seemed to prevent bortezomib from fighting the disease by blocking its proteasome inhibitory function – the two compounds effectively contradicted one another in the cell, leaving nearly 100 percent of the tumor cells intact.

Importantly, the team found that EGCG only reacted with proteasome inhibitors that have a boronic acid base (including bortezomib) but did not react with several non-boronic acid-based proteasome inhibitors (such as nelfinavir [Viracept®], a treatment for HIV). The researchers determined that the boronic acid in bortezomib helped to bind the EGCG directly to the therapy molecule, thereby cancelling out the effects of both the green tea and the therapy on the tumor cells.

The study findings may have several important implications in the clinical setting. The EGCG blocked bortezomib's antitumor effects at levels that are commonly achieved with the use of available concentrated

green tea supplements (as low as 2.5  $\mu\text{M}$  – which can be attained with two to three 250 mg capsules of green tea extract) suggesting the impact is very real for patients supplementing their therapy. The team also believes that as the EGCG inactivates bortezomib's function in the tumor cell, it may also prevent some of the side effects that usually accompany the therapy. As a result, patients taking green tea products to supplement their therapy may experience improved well being and feel encouraged to increase their intake while unknowingly blunting or completely negating the efficacy of their bortezomib treatment.

“Our surprising results indicate that green tea polyphenols may have the potential to negate the therapeutic efficacy of bortezomib,” said Dr. Schönthal. “The current evidence is sufficient enough to strongly urge patients undergoing bortezomib therapy to abstain from consuming green tea products, in particular the widely available, highly concentrated green tea and EGCG products that are sold in liquid or capsule form.”

The findings of the study are considered specific for patients taking bortezomib as opposed to any other common cancer therapy. The analysis of the study offered a clear understanding of the boronic acid-related mechanisms that cause the negative outcome, offering the conclusion that green tea would counteract most, if not all, compounds that work with boronic acid. However, while there are many chemicals that contain boronic acid, few are being used with patients.

“Although the study has exposed detrimental effects of green tea in specific combination with Velcade, this should not minimize the previously reported potentially beneficial effect of this herb,” said Dr. Schönthal. “Related studies with other types of cancer therapies are promising and green tea extract may actually improve the anticancer effects of other drugs.”

### **Don't go changing: New chemical keeps stem cells young**

Scientists at the Universities of Bath and Leeds have discovered a chemical that stops stem cells from turning into other cell types, allowing researchers to use these cells to develop new medical treatments more easily.

Stem cells have the ability to develop into many other cell types in the body, and scientists believe they have huge potential to treat diseases or injuries that don't currently have a cure.

Professor Melanie Welham's team at the University of Bath's Department of Pharmacy & Pharmacology, collaborating with Professor Adam Nelson at the University of Leeds, have discovered a chemical that can be added to embryonic stem cells grown in the lab, allowing them to multiply without changing into other cell types. This breakthrough will help scientists produce large stocks of cells that are needed for developing new medical therapies.

Professor Welham, who is co-director of the University of Bath's Centre for Regenerative Medicine, explained: “Stem cells have great potential for treating spinal injuries and diseases like type I diabetes because they can change into a range of specialised cell types including nerve or pancreatic cells, which could be used to repair damaged tissues.

“Unfortunately, when you grow stem cells in the lab, they can spontaneously develop into specialised cells, making it difficult to grow large enough stocks to use for medical research. “We've identified a chemical that will put this process on hold for several weeks so that we can grow large numbers of them in their unspecialised state. This is reversible, so when you take it away from the cells, they still have the ability to change into specialised cells.”

Professor Adam Nelson's team, at the Astbury Centre for Structural Molecular Biology, made more than 50 chemical compounds that were tested for activity in the stem cells. The researchers found that the chemicals worked by blocking an enzyme, called GSK3, that can control when the stem cell switches to a more specialised cell type.

Professor Nelson, who is Director of the Astbury Centre at the University of Leeds, said: “This research is a great example of how small molecules can be used as tools to understand biological mechanisms.”

*The research, supported by funding from the Biotechnology & Biological Sciences Research Council, is published in the prestigious peer-reviewed Cell Press journal, Chemistry & Biology.*

### **Nightmares increase risk of further suicide attempts**

A thesis from the Sahlgrenska Academy, University of Gothenburg, Sweden, concludes that people who have nightmares following a suicide attempt are five times more likely to attempt suicide again, compared with those who do not have nightmares.

The study included 165 patients aged 18-69 years, who were being treated at somatic and psychiatric departments following a suicide attempt in Sweden. Psychiatric interviews and self-assessments were carried out as part of the study during the week following the suicide attempt, and then two months later. Ninety-eight people attended the follow-up interview.

The study shows that those patients who complained of nightmares during the week following the suicide attempt were three times more likely to attempt to take their own life again, regardless of gender or psychiatric diagnosis, such as depression or post-traumatic stress syndrome.

"Those who were still suffering from nightmares after two months faced an even greater risk. These people were five times more likely to attempt suicide a second time," says author of the thesis, Registered Nurse Nils Sjöström.

### **Other sleeping difficulties do not increase risk of repeat suicide attempts**

It is normal for patients that have attempted suicide to suffer from sleeping difficulties. Some 89 percent of the patients examined reported some kind of sleep disturbance. The most common problems were difficulty initiating sleep, followed by difficulty maintaining sleep, nightmares and early morning awakening. Nils Sjöström has also examined the possibility of there being an increased risk of repeat suicide attempts if the patient has difficulty falling asleep, difficulty sleeping during the night, or wakes up early in the morning. However, the result did not indicate any increased risk.

"The results show how important it is for healthcare staff to highlight the significance of nightmares in the clinical suicide risk assessment," says Nils Sjöström.

*Thesis for the degree of Doctor of Medicine at the Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Sweden.*

*Title of thesis: Sleep, sense of coherence and suicidality in suicide attempters*

## **Study finds Zen meditation alleviates pain**

### **University of Montreal pain management study in Psychosomatic Medicine**

Montreal, February 3, 2009 – Zen meditation – a centuries-old practice that can provide mental, physical and emotional balance – may reduce pain according to Université de Montréal researchers. A new study in the January edition of Psychosomatic Medicine reports that Zen meditators have lower pain sensitivity both in and out of a meditative state compared to non-meditators.

Joshua A. Grant, a doctoral student in the Department of Physiology, co-authored the paper with Pierre Rainville, a professor and researcher at the Université de Montréal and its affiliated Institut universitaire de gériatrie de Montréal. The main goal of their study was to examine whether trained meditators perceived pain differently than non-meditators.

"While previous studies have shown that teaching chronic pain patients to meditate is beneficial, very few studies have looked at pain processing in healthy, highly trained meditators. This study was a first step in determining how or why meditation might influence pain perception," says Grant.

### **Meditate away the pain**

For this study, the scientists recruited 13 Zen meditators with a minimum of 1,000 hours of practice to undergo a pain test and contrasted their reaction with 13 non-meditators. Subjects included 10 women and 16 men between the ages of 22 to 56.

The administered pain test was simple: A thermal heat source, a computer controlled heating plate, was pressed against the calves of subjects intermittently at varying temperatures. Heat levels began at 43 degrees Celsius and went to a maximum of 53 degrees Celsius depending on each participant's sensitivity. While quite a few of the meditators tolerated the maximum temperature, all control subjects were well below 53 degrees Celsius.

Grant and Rainville noticed a marked difference in how their two test groups reacted to pain testing – Zen meditators had much lower pain sensitivity (even without meditating) compared to non-meditators. During the meditation-like conditions it appeared meditators further reduced their pain partly through slower breathing: 12 breaths per minute versus an average of 15 breaths for non-meditators.

"Slower breathing certainly coincided with reduced pain and may influence pain by keeping the body in a relaxed state," says Grant. "While previous studies have found that the emotional aspects of pain are influenced by meditation, we found that the sensation itself, as well as the emotional response, is different in meditators."

The ultimate result? Zen meditators experienced an 18 percent reduction in pain intensity. "If meditation can change the way someone feels pain, thereby reducing the amount of pain medication required for an ailment, that would be clearly beneficial," says Grant.

*Partners in research: This study was funded by the Canadian Institutes of Health Research, the Mind and Life Institute Varela Grant (J.A.G.) and the Fonds de la recherche en santé du Québec.*

### **On the Web:**

*About the cited article in Psychosomatic Medicine: [www.psychosomaticmedicine.org/cgi/content/abstract/71/1/106](http://www.psychosomaticmedicine.org/cgi/content/abstract/71/1/106)*

*About the Université de Montréal: [www.umontreal.ca/english/index.htm](http://www.umontreal.ca/english/index.htm)*

*About the Department of Physiology: [www.physio.umontreal.ca](http://www.physio.umontreal.ca)*

*About Pierre Rainville: [www.criugm.qc.ca/a\\_chercheur.html?id=114](http://www.criugm.qc.ca/a_chercheur.html?id=114)*

*About the Mind and Life Institute: [www.mindandlife.org](http://www.mindandlife.org)*

About the health benefits of meditation according to the U.S. National Center for Complementary and Alternative Medicine: <http://nccam.nih.gov/health/meditation/overview.htm>

Note: A video-report about this research can be viewed at <http://ca.youtube.com/watch?v=SNAtLpwgey8>.

## **Neural mapping paints a haphazard picture of odor receptors**

### **Arrangement of receptors appears uniformly random across individuals and species**

CAMBRIDGE, Mass.-- Despite the striking aromatic differences between coffee, peppermint, and pine, a new mapping of the nose's neural circuitry suggests a haphazard patchwork where the receptors for such disparate scents are as likely as not to be neighbors.

Inexplicably, this seemingly random arrangement is faithfully preserved across individuals and even species, with cells that process the same scent located in precisely the same location on the olfactory bulb, the brain's first processing station for odors.

The crazy-quilt map of odor-processing neurons on the front lines of the olfactory system is described by Harvard University neuroscientists in the February issue of the journal *Nature Neuroscience*.

"It had been thought that the layout of the olfactory bulb was variable from individual to individual, but followed a chemotopic order where cells handling similar odor responses are near each other," says Markus Meister, the Jeff C. Tarr Professor of Molecular and Cellular Biology in Harvard's Faculty of Arts and Sciences. "Here we show that the layout is actually very precise -- the same from animal to animal -- but doesn't appear to follow any chemotopic order whatsoever."

Working with mice and rats, Meister and colleague Venkatesh N. Murthy recorded neural responses to several hundred distinct odors, including anise, beer, cloves, coffee, ginger, lemon, orange, peppermint, pine, rose, and even fox pheromones. The neuroscientists found that across individuals and even across the two species, bundles of neurons from a given type of odor receptor -- known as glomeruli -- were found in almost exactly the same spot on the olfactory bulb, a sensory structure measuring some four to five millimeters across and located at the very front of the brain.

"Glomeruli from different receptors line the surface of the olfactory bulb like an array of close-packed marbles," says Murthy, professor of molecular and cellular biology at Harvard. "Across individuals the location of a given glomerulus varies by only one array position. Compared to the size of the map, this represents a remarkable developmental precision of one part in 1,000."

Meister and Murthy then analyzed whether nearby glomeruli detect similar odors, such as those with similar chemical structures. Neuroscientists have previously hypothesized axes of similarities along which odors might be classified.

"One might expect that nearby glomeruli should have similar odor sensitivities," Meister says, "but we were surprised to find this was not the case. The odor response spectra of two neighboring glomeruli were as dissimilar as those of distant glomeruli."

This seemingly haphazard layout of sensory properties stands in marked contrast to other brain maps, such as those governing vision, touch, and hearing. In these three cases, our brains represent the outside world using ordered maps -- such as when neighboring points in visual space activate neighboring points on the retina.

"That sort of arrangement makes sense, since most brain computation is local, relying on short connections between nearby cells," Murthy says. "This is necessary because the connections between neurons occupy most of the volume available to the brain, and long-distance connections require more of this volume."

Meister and Murthy suspect that the deliberate randomness in rodents' odor maps is likely also found in humans, which have only one-third as many receptors but are capable, in some extreme cases, of discerning tens of thousands of distinct smells.

*Meister and Murthy's co-authors on the Nature Neuroscience paper are Edward R. Soucy, Dinu F. Albeanu, and Antoniu L. Fantana, all of Harvard's Department of Molecular and Cellular Biology and Center for Brain Science. Their work was funded by Harvard University.*

## **Mayo Clinic Researchers Suspect a Novel Gene is Causing Restless Legs Syndrome in a Large Family**

JACKSONVILLE, Fla. — In 2005, a woman who had trouble sleeping asked Siong-Chi Lin, M.D., for help. Dr. Lin, a sleep disorders specialist at the Mayo Clinic campus in Florida, diagnosed restless legs syndrome. This common neurologic disorder interrupts sleep because of unpleasant sensations in the legs at rest, especially in the evening, that are temporarily relieved by movement.

Restless legs syndrome affects between 5 and 11 percent of the population in North America and Europe, says Dr. Lin. The cause may be a number of clinical factors, such as iron deficiency, but it has a strong genetic component as well. "In most people, it is likely due to a number of different causes, but genes are very likely the most important factor in affected families," he says.



Medications, especially agents that increase transmission of dopamine in brain neurons, are effective in many people and worked for his new patient, says Dr. Lin. "The syndrome may appear as a nuisance for most people, however it can also seriously affect some people's quality of life," he says.

Dr. Lin's patient told him that many of her relatives also have the same trouble sleeping — difficulties she could trace back through her ancestry.

With the patient's approval, that information was relayed to "gene hunters" in Mayo Clinic's neurosciences department. These investigators have established an international reputation for their ability to find the genetic roots of rare, as well as common, neurological disorders. Dr. Lin accompanied investigators to Indiana, the hub of the extended family, which is believed to be of English descent, to interview dozens of individuals spanning multiple generations. They found that 30 relatives were affected by restless legs syndrome, and discovered that almost three times as many females had the condition compared to males.

Now, the researchers are reporting in the February issue of Mayo Clinic Proceedings that the restless legs syndrome found in this family is likely due to a gene mutation that has never been linked to the disorder.

To date, five loci, or areas on the genome, have been linked to restless legs syndrome in other families around the world, but this family does not have any of those mutations.

"That means this family likely has a novel gene that is causing the disease," says the study's lead investigator, Carles Vilariño-Güell, Ph.D., a neuroscientist at Mayo Clinic's campus in Jacksonville. The researchers have not yet pinpointed the culprit gene, but say they are getting close.

This study is important, Dr. Vilariño-Güell says, because this family is one of the largest with restless legs syndrome ever studied, and the disorder spans multiple generations. Therefore, the gene linked to the syndrome is widespread among the affected relatives, increasing the chances that the researchers will soon zero in on the gene responsible.

"With so many people in this family affected by the syndrome, we have a lot of power to find the gene mutation causing disease," he says.

Once a gene is discovered, researchers can investigate its normal function and the mutation's effect, and then can "try to overcome that problem with drug therapy," he says. They can also trace the molecular route from the gene mutation to the disorder, and see if the other loci linked to the syndrome lie along this pathway. So far, no one has found a definitive link between restless legs syndrome and a specific gene mutation, but large families hold the clues for these discoveries, says Dr. Vilariño-Güell.

*Co-authors of the study include Matthew Farrer, Ph.D., and Zbigniew Wszolek, M.D.*

*The study was funded by The Mayo Foundation Research Committee, the National Institutes of Health, and the Pacific Alzheimer Research Foundation.*

## **Breast cancer risk rapidly declines after women stop taking postmenopausal combined hormone therapy**

### ***Women's Health Initiative study published in the New England Journal of Medicine***

LOS ANGELES – Women who stopped taking the postmenopausal hormone combination of estrogen plus progestin experienced a marked decline in breast cancer risk which was unrelated to mammography utilization change, according to a study from the Women's Health Initiative led by a Los Angeles Biomedical Research Institute (LA BioMed) investigator that was published today in *The New England Journal of Medicine*.

"These findings support the hypothesis that the recent reduction in breast cancer incidence in the United States is predominantly related to a decrease in combined estrogen plus progestin use," said Rowan T. Chlebowski, M.D., Ph.D., a LA BioMed chief investigator and lead author for the study.

Breast cancer in the United States began to decline in 2003, after the Women's Health Initiative's initial findings that combined hormone therapy was related to higher risk of breast cancer and heart problems.

Using data from the Women's Health Initiative's randomized trial and observational study cohort of postmenopausal women on combined hormone therapy, the researchers in the study published today also found that continued use of combined estrogen plus progestin after five years about doubles subsequent breast cancer risk each year.

"Postmenopausal women and their physicians should consider these findings in weighing the risks and benefits of combined estrogen plus progestin use, especially if the women plan to take the medication for more than five years," said Dr. Chlebowski.

## **Primitive whales gave birth on land**

\* 00:01 04 February 2009 by Ewen Callaway and Catherine Brahic

The first whales gave birth on land, suggests a unique 47 million-year-old fossil of a pregnant female. The discovery provides the first concrete proof to a long-standing theory that the ancestors of whales lived something of a double life, moving back and forth between land and sea.

"These were speculations. I never thought we'd get evidence for or against," says Philip Gingerich, a palaeontologist at the University of Michigan in Ann Arbor, whose team found the fossilised mother and calf in north-eastern Pakistan.

As if that wasn't enough, Gingerich's team also unearthed a nearly complete fossil - "right down to the end of the tail," he says - belonging to a male of the same species, *Maicatetus inuus*.

Together, the fossils shed light on the earliest stages of whale evolution, when the [descendants of hoofed deer-like animals took to the sea](#).



*The earliest whales may not have lost their links to land* (Image: John Klausmeyer)

### Head first

The first whales, known as protocetids, did not fully embrace their new ocean habitat. They probably stuck close to shore and made occasional trips back to the land, Gingerich says.

"They certainly weren't walking," he says. "They were more like sea lions, which can move more than you would think from their morphology."

Also like sea lions, *Maicatetus* gave birth on land. The fossilised calf's head faces outward from the uterus, which is how all land mammals give birth. Whales and dolphins, on the other hand, deliver their calves tail first - possibly so they don't drown before the end of labour.

The fossilised fetus also has developing molar teeth, an indication that it was well-developed when it was born. "Anything that is born with molars ... is born ready to live in open environments", and perhaps able to evade predators, Gingerich says.

He adds that he has no idea what killed the ancestral whales.

### Unique find

Mark Uhen, a vertebrate palaeontologist at the University of Alabama in Tuscaloosa is excited by the new fossil. "I've searched through every piece of literature on fossil whales on the planet. I've never seen a fetus inside a mother," he says.

It is now important to find fossils that fill in the final details of whales' slow march to the sea, Uhen says. "I hope we find more of this sort of thing." *Journal reference: PLoS ONE (DOI: 10.1371/journal.pone.0004366)*

### Mind

## The Muddled Tracks of All Those Tears

By BENEDICT CAREY

They're considered a release, a psychological tonic, and to many a glimpse of something deeper: the heart's own sign language, emotional perspiration from the well of common humanity.

Tears lubricate love songs and love, weddings and funerals, public rituals and private pain, and perhaps no scientific study can capture their many meanings.

"I cry when I'm happy, I cry when I'm sad, I may cry when I'm sharing something that's of great significance to me," said Nancy Reiley, 62, who works at a women's shelter in Tampa, Fla., "and for some reason I sometimes will cry when I'm in a public speaking situation.



Jonathon Rosen

It has nothing to do with feeling sad or vulnerable. There's no reason I can think of why it happens, but it does."

Now, some researchers say that the common psychological wisdom about crying — crying as a healthy catharsis — is incomplete and misleading. Having a "good cry" can and usually does allow people to recover some mental balance after a loss. But not always and not for everyone, argues a review article in the current issue of the journal *Current Directions in Psychological Science*. Placing such high expectation on a tearful breakdown most likely sets some people up for emotional confusion afterward.

This call for a more nuanced view of crying stems partly from a critique of previous studies. Over the years, psychologists have confirmed many common observations about crying. It is infectious. Women break down more easily and more often than men, for reasons that are very likely biochemical as well as cultural. And the physical experience mirrors the psychological one: heart rate and breathing peak during the storm and taper off as the sky clears.

When asked about tearful episodes, most people, as expected, insist that the crying allowed them to absorb a blow, to feel better and even to think more clearly about something or someone they had lost.

At least that's the way they remember it — and that's the rub, said Jonathan Rottenberg, a psychologist at the University of South Florida and a co-author of the review paper. "A lot of the data supporting the conventional wisdom is based on people thinking back over time," he said, "and it's contaminated by people's beliefs about what crying should do."

Just as researchers have found that people tend, with time, to selectively remember the best parts of their vacations (the swim-up bars and dancing) and forget the headaches, so crying may also appear cathartic in retrospect. Memory tidies up the mixed episodes — the times when tears brought more shame than relief, more misery than company.

In a study published in the December issue of *The Journal of Social and Clinical Psychology*, Dr. Rottenberg, along with Lauren M. Bylsma of the University of South Florida and Ad Vingerhoets of Tilburg University in the Netherlands, asked 5,096 people in 35 countries to detail the circumstances of their most recent crying episode. About 70 percent said that others' reactions to their breakdown were positive, comforting. But about 16 percent cited nasty or angry reactions that, no surprise, generally made them feel worse.

Given that the most obvious social function of crying is to rally support and sympathy, the emotional impact of the tears depends partly on who is around and what they do. The study found crying with just one other person present was significantly more likely to produce a cathartic effect than doing so in front of a larger group. "Almost all emotions are, at some level, directed at others, so their response is going to be very important," said James J. Gross, a psychologist at Stanford.

The experience of crying also varies from person to person, and some are more likely than others to find catharsis. In laboratory studies, psychologists induce crying by showing participants short clips of very sad movie scenes, like from "The Champ" or "Steel Magnolias." Those who break down — typically about 40 percent of women, very few men — then report directly on the experience. These kinds of studies, though no more than a simulation of lived experience, suggest that people with symptoms of depression and anxiety do not get as worked up, nor recover as fast, as most people do. In surveys, they are also less likely than most to report psychological benefits from crying.

People who are confused about the sources of their own emotions — a condition that in the extreme is called alexithymia — also tend to report little benefit from a burst of tears, studies have found. This makes some sense. One purpose of crying may be to block thinking, to effectively seal off the flood of unanswerable questions that come after any major loss, the better to clarify those that are most important or most practical. If this psychological system is already clunky, a fire shower of tears is not likely to improve it.

In her book "Seeing Through Tears: Crying and Attachment," Judith Kay Nelson, a therapist and teacher living in Berkeley, Calif., argues that the experience of crying is rooted in early childhood and people's relationship with their primary caregiver, usually a parent. Those whose parents were attentive, soothing their cries when needed, tend to find that crying also provides them solace as adults. Those whose parents held back, or became irritated or overly upset by the child's crying, often have more difficulty soothing themselves as adults.

"Crying, for a child, is a way to beckon the caregiver, to maintain proximity and use the caregiver to regulate mood or negative arousal," Dr. Nelson said in a phone interview.

Those who grow up unsure of when or whether that soothing is available can, as adults, get stuck in what she calls protest crying — the child's helpless squall for someone to fix the problem, undo the loss.

"You can't work through grief if you're stuck in protest crying, which is all about fixing it, fixing the loss," Dr. Nelson said. "And in therapy - as in close relationships - protest crying is very hard to soothe, because you can't do anything right, you can't undo the loss. On the other hand, sad crying that is an appeal for comfort from a loved one is a path to closeness and healing."

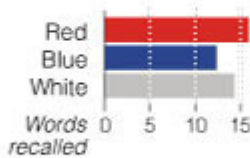
Tears can cleanse, all right. But like a flash flood, they may also leave a person feeling stranded, and soaked.

### Seeing Red, Seeing Blue

A study of 600 people who performed tasks on computer screens with red, blue or neutral backgrounds found that the red group did better on tests of attention to detail, while the blue group did better at creative tasks.

#### RECALLING WORDS

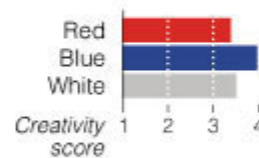
Some participants were asked to complete a detail-orientated task: studying and later recalling a list of 36 words. People in the red group recalled more words correctly than those in the blue group, with fewer false recollections.



Source: Science

#### THINKING CREATIVELY

Other participants tried a creative task, thinking of as many creative uses as possible for a brick. Each group produced the same number of suggestions, but a panel of judges rated those of the blue group to be the most creative.



THE NEW YORK TIMES

## Reinvent Wheel? Blue Room. Defusing a Bomb? Red Room.

By PAM BELLUCK

Trying to improve your performance at work or write that novel? Maybe it's time to consider the color of your walls or your computer screen.

If a new study is any guide, the color red can make people's work more accurate, and blue can make people more creative.

In the study, published Thursday on the Web site of the journal *Science*, researchers at the University of British Columbia conducted tests with 600 people to determine whether cognitive performance varied when people saw red or blue. Participants performed tasks with words or images displayed against red, blue or neutral backgrounds on computer screens.

Red groups did better on tests of recall and attention to detail, like remembering words or checking spelling and punctuation. Blue groups did better on tests requiring imagination, like inventing creative uses for a brick or creating toys from shapes.

"If you're talking about wanting enhanced memory for something like proofreading skills, then a red color should be used," said Juliet Zhu, an assistant professor of marketing at the business school at the University of British Columbia, who conducted the study with Ravi Mehta, a doctoral student.

But for "a brainstorming session for a new product or coming up with a new solution to fight child obesity or teenage smoking," Dr. Zhu said, "then you should get people into a blue room."

The question of whether color can color performance or emotions has fascinated scientists, not to mention advertisers, sports teams and restaurateurs.

In a study on Olympic uniforms, anthropologists at Durham University in England found that evenly matched athletes in the 2004 Games who wore red in boxing, taekwondo, Greco-Roman wrestling and freestyle wrestling defeated those wearing blue 60 percent of the time. The researchers suggested that red, for athletes as for animals, subconsciously symbolizes dominance.

Effects that were perhaps similarly primal were revealed in a 2008 study led by Andrew Elliot of the University of Rochester. Men considered women shown in photographs with red backgrounds or wearing red shirts more attractive than women with other colors, although not necessarily more likeable or intelligent.

Then there was the cocktail party study, in which a group of interior designers, architects and corporate color scientists built model rooms decorated as bars in red, blue or yellow. They found that more people chose the yellow and red rooms, but that partygoers in the blue room stayed longer. Red and yellow guests were more social and active. And while red guests reported feeling hungrier and thirstier than others, yellow guests ate twice as much.

Experts say colors may affect cognitive performance because of the moods they engender.

"When you feel that the situation you are in is problematic," said Norbert Schwarz, a psychology professor at the University of Michigan, "you are more likely to pay attention to detail, which helps you with processing tasks but interferes with creative types of things."

By contrast, Dr. Schwarz said, "people in a happy mood are more creative and less analytic."

Many people link red to problematic things, like emergencies or X's on failing tests, experts say. Such "associations to red — stop, fire, alarm, warning — can be activated without a person's awareness, and then influence what they are thinking about or doing," said John A. Bargh, a psychology professor at Yale University. "Blue seems a weaker effect than red, but blue skies, blue water are calm and positive, and so that effect makes sense too."

Still, Dr. Schwarz cautioned, color effects may be unreliable or inconsequential. "In some contexts red is a dangerous thing, and in some contexts red is a nice thing," he said. "If you're walking across a frozen river, blue is a dangerous thing."

Indeed, Dr. Elliot of the University of Rochester said blue's positive emotional associations were considered less consistent than red's negative ones.

It might also matter whether the color dominates someone's view, as on a computer screen, or is only part of what is seen. Dr. Elliot said that in the *Science* study, brightness or intensity of color - not just the color itself - might have had an effect.

Some previous cognitive studies found no effect from color, although some used mostly pastels or less distinctive tasks. One found that students taking tests did better on blue paper than on red, but Dr. Schwarz said the study used depressing blue and upbeat red.

The *Science* study's conclusion that red makes people more cautious and detail-oriented coincides with Dr. Elliot's finding that people shown red test covers before I.Q. tests did worse than those shown green or neutral

colors. And on a different test, people with red covers also chose easier questions. I.Q. tests require more problem-solving than Dr. Zhu's memory and proofreading questions.

When Dr. Zhu's subjects were asked what red or blue made them think of, most said that red represented caution, danger or mistakes, and that blue symbolized peace and openness. Subjects were quicker to unscramble anagrams of "avoidance related" words like "danger" when the anagrams were on red backgrounds, and quicker with anagrams of positive, "approach related" words like "adventure" when they were on blue backgrounds.

The study also tested responses to advertising, finding that advertisements listing product details or emphasizing "avoidance" actions like cavity prevention held greater appeal on red backgrounds, while ones using creative designs or emphasizing positive actions like "tooth whitening" held more appeal on blue.

When the participants were asked if they believed red or blue would improve performance, most said blue for both detail-oriented and creative tasks. Maybe, Dr. Zhu said, that is because more people prefer blue.

The study did not involve different cultures, like China, where red symbolizes prosperity and luck. And it said nothing about mixing red and blue to make purple.

For what it's worth, many newsroom walls at The New York Times are bright tomato-soup red. The newspaper's facilities department says there are no blue rooms in the place.

### **Ancient sponges leave their mark**

**By Jonathan Amos** Science reporter, BBC News

Traces of animal life have been found in rocks dating back 635 million years.

The evidence takes the form of chemical markers that are highly distinctive of sponges when they die and their bodies break down in rock-forming sediments.

The discovery in Oman pushes back the earliest accepted date for animal life on Earth by tens of millions of years.

Scientists tell Nature magazine that the creatures' existence will help them understand better what the planet looked like all that time ago.

"The fact that we can detect these signals shows that sponges were ecologically important on the seafloor at that time," said lead author Gordon Love, from the University of California, Riverside.

"We're not saying we captured the first animal; we're saying they're an early animal phylum and we're capturing them when their biomass was significant."



*The rocks date to a time of dramatic glaciation on Earth*

### **Tiny creatures**

Researchers can usually determine the presence of ancient life in rock strata by looking for the fossilised remains of skeletons or the hardened record of the creatures' movements, such as their footprints or crawl marks.

But for organisms deep in geological history that were extremely small and soft bodied, scientists have had to develop novel techniques to uncover their existence.

One of these newer methods involves detecting breakdown products from the lipid molecules which act as important structural components in the cell membranes of animals.

Over time, these will transform to leave a molecule known as cholestrane; and for sponges, this exclusively takes the form known as 24-isopropylcholestane.

Dr Love's team found high concentrations of this biomarker in rocks located at the south-eastern edge of the Arabian peninsula.

They were laid down in what would have been a shallow marine environment at least 635 million years ago.

"Even though there must have been sufficient oxygen in the water to maintain the metabolism of these primitive animals, I think their size would have been restricted by oxygen being nowhere near modern values," the UC Riverside researcher said.

"We're probably talking about small colonies of sponges with body dimensions of a few millimetres at most. They'd have been filtering organic detritus in the water column."

### **Icy planet**

The discovery is fascinating because it pre-dates the end of the Marinoan glaciation, a deep freeze in Earth history that some argue shrouded the entire planet in ice.

Scientists often refer to the term "snowball Earth" to describe conditions at this time.

So to find animal life apparently thriving during this glaciation seems remarkable, commented Jochen Brochs, from the Australian National University, Canberra.

"If there really was a snowball Earth, how did those sponges survive? The full snowball Earth hypothesis would predict that the oceans were frozen over by 2km, even at the equator," he told BBC News.

"Only at hot springs could any organism survive but it is questionable that you would have sponges in a hot spring. I haven't made my mind up about snowball Earth but perhaps these sponges are telling us something about this glaciation."

Dr Love's view is that the presence of these animals puts limits on the scale of the ice coverage.

"I believe there were areas of what we might call refugia - areas of open ocean where biology could go on. And in this case, it could be evidence that we had some sort of evolutionary stimulation of new grades of organisms as well." *Jonathan.Amos-INTERNET@bbc.co.uk*

### **Discovery by Brown Researchers Could Lead to New Autism Treatment**

***A Brown research team led by neuroscience professor Justin Fallon has discovered a structure in the brain called the Fragile X granule, which offers a potential target for treating certain kinds of autism and mental retardation. Details were published Feb. 4, 2009, in the Journal of Neuroscience.***

PROVIDENCE, R.I. [Brown University] — A Brown University research team has discovered something in the brain that could serve as a target for future autism and mental retardation treatments.

Discovery of the novel Fragile X granule is detailed in the Feb. 4, 2009, issue of the Journal of Neuroscience. This finding opens a new line of research about potential treatments for autism, a neurological disorder that strikes young children and can impair development of social interaction and communication.

"If you are going to treat the disease you need to be able to target the defective elements," said Justin Fallon, professor of neuroscience at Brown. "The Fragile X granule offers such a target."

Fallon is senior author of the paper titled "The FXG: A presynaptic Fragile X granule expressed in a subset of developing brain circuits." Two postdoctoral students at Brown served as lead authors: Sean Christie and Michael Atkins. James Schwob, a researcher from Tufts University Medical School, also participated.

Autism affects as many as 1.5 million Americans, and the number is increasing, according to the Autism Society of America. It is estimated that 1 in 150 births involve children with some form of autism.

Autism can be caused by a variety of genetic factors, but Fallon's lab focused on one particular area — the Fragile X protein. If that protein is mutated, it leads to Fragile X syndrome, which causes mental retardation and is often accompanied by autism.

There is growing recognition in the field that autism and mental retardation are diseases of the synapse, the basic unit of information exchange and storage in the brain. Many groups have extensively studied the role of the Fragile X protein in the post-synaptic, or receiving side of synaptic connections. This was a starting point for the research conducted by Fallon's team in their study of the Fragile X protein and synaptic connections in healthy mice.

By examining specially prepared sections of mouse brain tissue with high-powered light and electron microscopes, Fallon's team made a number of determinations. First, they showed that Fragile X exists at the pre-synaptic, or sending side of the synapse. This is an area that had not been widely studied.

"For over 25 years the field has focused almost exclusively on the post-synaptic, receiving side," Fallon said. "Almost no one has looked at the pre-synaptic side, as it was not thought to be involved in Fragile X."

This discovery is important because scientists, if they are to treat Fragile X syndrome, autism or mental retardation must know where the functional defect actually is. Fallon's research helps fill in a potential gap. "The implication is that pre-synaptic defects could contribute to the pathology in autism in Fragile X," Fallon said.

Even more significantly, Fallon and his lab learned that Fragile X protein is only present in a small fraction of what are known as pre-synaptic specializations. The pre-synaptic Fragile X protein also turned out to be present in microscopic granules, which look like tiny pebbles under a high-powered microscope. Understanding the Fragile X granule is important in this context because the finding could lead to more targeted treatments.

Further research is needed, but Fallon's lab hypothesizes that the granules contain multiple RNAs, or sets of genetic information to help modify the synapse during learning and memory. If their theory is proven correct, the granules might serve as pinpoint targets for eventual drug treatments of autism.

The scientists' efforts date to 2005; their finding of the Fragile X granules was "serendipity," Fallon said. The original focus was on developing an improved method for visualizing where Fragile X protein sits in the brain. That new visualization method led to the discovery of the granules.

*The work was supported by the National Institutes of Health and FRAXA, the Fragile X Research Foundation.*

## **The nonsense in our genes** **1 in 200 human genes superfluous?**

1 in 200 of our human genes can be inactivated with no detectable effect on our health. A study by Wellcome Trust Sanger Institute scientists raises new questions about the effects of gene loss on our wellbeing and evolution.

The study, published today in *The American Journal of Human Genetics*, explores single letter changes in our genetic code that affect the ability of genes to produce proteins. The researchers' findings suggest that such mutations, while sometimes harmful, generally have little consequence for the individual and may occasionally even be beneficial in evolutionary terms.

The team studied variations in the genetic code of more than 1000 people from around the world. They focused their work on single-letter changes (called SNPs) that disrupt proteins, leading to versions that are either shorter or completely absent. One might intuitively expect that such a change - called a nonsense-SNP - would be harmful to the person.

"We knew that these mutations existed and that many have been associated with genetic diseases, but we were amazed to find that they were so common in the general population," said Bryndis Yngvadottir, lead author on the study. "We found that 167 genes could be inactivated by nonsense mutations, and that individuals carry on average at least 46 such variations. For 99 of the genes, both copies could be lost in adults living a normal existence."

Human DNA contains approximately 20,000 genes: the total of 99 genes with nonsense-SNPs means that at least 1 in 200 genes is dispensable. Some harmful nonsense-SNPs were also present among the 167 genes studied: 8 are listed in the Human Gene Mutation Database which catalogues disease-causing mutations.

While the researchers found that inactivating genes was, on the whole, slightly harmful, there were exceptions. In East Asia, but not in other places, it seems to have been advantageous to lose the *MAGEE2* gene.

"There is a theory that 'less is more' where genes are concerned" explained the study's coordinator, Chris Tyler-Smith, "and we already knew of a couple of examples of advantageous gene loss. But this is the first large-scale investigation of its significance for recent human evolution.

"The *MAGEE2* gene is an interesting new example, although we have absolutely no idea what this gene does, or why some people are better off without it. However, our study suggests that overall, gene loss has not been a major evolutionary force: our genome does not seem to be in a hurry to get rid of these 'superfluous' genes."

"Certain types of genes tend to be lost preferentially. We found the biggest decrease in the genes that contribute to our sense of smell. Perhaps early humans didn't like smelly partners, and so when humans started to live together in big groups it helped their chances of finding true love if they couldn't smell their partner too strongly," speculated Bryndis Yngvadottir.

Genetic variation in nonsense-SNP numbers was significant: participants in the survey had between 29 and 65 of these mutations each and varied on average by 24 genes as a consequence. 18 of the 169 nonsense-SNPs investigated are also present in the Craig Venter genome published last year.

### *Notes to Editors Publication Details*

*Yngvadottir B et al. (2009) A genomewide survey of the prevalence and evolutionary forces acting on human nonsense-SNPs. The American Journal of Human Genetics.*

## **Scientists propose new direction in the search for genetic causes of schizophrenia**

A new study shows that schizophrenia is caused, at least in part, by large, rare structural changes in DNA referred to as copy number variants (CNVs) – not the tiny, single letter alterations (single nucleotide polymorphisms (SNPs) that scientists have pursued for years. The findings are published February 6 in the open-access journal *PLoS Genetics*.

Schizophrenia is one of the most common psychiatric disorders, but scientists have yet to determine significant genetic links. Over the past two decades, dozens of genes and SNPs have been identified as possible candidates, but the current study dismisses them.

"The literature is replete with dozens of genes and SNPs identified as associated with schizophrenia," says first author Anna Need, PhD, a postdoctoral associate in the Center for Human Genome Variation at the Duke Institute for Genome and Sciences Policy. "But we systematically retested all the leading candidates and concluded that most, if not all of them, are false positives." Need says she believes the previous studies were too small to properly assess the role of SNPs.

Need worked with senior author David Goldstein, of the Center for Human Genome variation, and a team of geneticists to scan the genome of schizophrenia patients and healthy controls for SNPs and copy number variants (CNVs). While none of the previously heralded SNPs appeared significant in schizophrenia, several CNVs emerged as potentially causative.

Copy number variants are common throughout the genome, usually appearing as deletions or duplications of significant stretches of DNA. They come in all sizes, but Goldstein says it is the largest deletions – those over two million bases long – that appear only in people with schizophrenia, and may be unique and causative in those individuals.

In schizophrenia patients, the researchers found eight such deletions, of which two were newly identified. While CNVs have been previously implicated in schizophrenia and other psychiatric conditions, the Duke researchers are the first to propose that the rarity of extremely large deletions suggest they are indeed pathogenic, at least in a small number of patients.

"What this means is that if we are going to make real headway in assessing genetic links to schizophrenia, we will have to sequence the entire genome of each schizophrenia patient," says Goldstein. "That is a tremendous amount of work, but it is the only way we will be able to find these extremely rare variations."

*CITATION: Need AC, Ge D, Weale ME, Maia J, Feng S, et al. (2009) A Genome-Wide Investigation of SNPs and CNVs in Schizophrenia. PLoS Genet 5(2): e1000373. doi:10.1371/journal.pgen.1000373  
<http://www.plosgenetics.org/article/info:doi/10.1371/journal.pgen.1000373>*

### **Genetic study shows direct link between vitamin D and MS susceptibility 'gene'**

Researchers have found evidence that a direct interaction between vitamin D and a common genetic variant alters the risk of developing multiple sclerosis (MS). The research, published on 6 February in the open-access journal PLoS Genetics, suggests that vitamin D deficiency during pregnancy and the early years may increase the risk of the offspring developing MS later in life.

MS is the most common disabling neurological condition affecting young adults. More than 85,000 people in the UK and 2.5 million worldwide are thought to suffer from the condition, which results from the loss of nerve fibres and their protective myelin sheath in the brain and spinal cord, causing neurological damage.

The causes of MS are unclear, but it has become evident that both environmental and genetic factors play a role. Previous studies have shown that populations from Northern Europe have increased MS risk if they live in areas receiving less sunshine. This supports a direct link between deficiency in vitamin D, which is produced in the body through the action of sunlight, and increased risk of developing the disease.

The largest genetic effect by far comes from the region on chromosome six containing the gene variant known as DRB1\*1501 and from adjacent DNA sequences. Whilst one in 1,000 people in the UK are likely to develop MS, this number rises to around one in 300 amongst those carrying a single copy of the variant and one in 100 of those carrying two copies.

Now, in a study funded by the UK's MS Society, the MS Society of Canada, the Wellcome Trust and the Medical Research Council, researchers at the University of Oxford and the University of British Columbia have established a direct relationship between DRB1\*1501 and vitamin D.

The researchers found that proteins activated by vitamin D in the body bind to a particular DNA sequence lying next to the DRB1\*1501 variant, in effect switching the gene on.

"In people with the DRB1 variant associated with MS, it seems that vitamin D may play a critical role," says co-author Dr Julian Knight. "If too little of the vitamin is available, the gene may not function properly."

"We have known for a long time that genes and environment determine MS risk," says Professor George Ebers, University of Oxford. "Here we show that the main environmental risk candidate – vitamin D – and the main gene region are directly linked and interact."

Professor Ebers and colleagues believe that vitamin D deficiency in mothers or even in a previous generation may lead to altered expression of DRB1\*1501 in offspring.

The finding – that the environment interacts directly with the background genetics of MS – complements research recently published in Human Molecular Genetics by Professor Ebers's group. There, they showed that environment changes to the same gene region can increase the risk of developing MS even further and can be inherited. These so-called "epigenetic effects" are being seen as increasingly important by scientists and there may be ways in which the effects reported in these two papers are related.

"Epigenetics will have important implications, not only for MS, but for other common diseases," says Professor Ebers. "For mothers, taking care of their health during their reproductive years may have beneficial effects on the health of their future children or even grandchildren."

The authors hypothesise that this gene-environment interaction may affect the ability of the thymus, a key component of the immune system, to perform its regular tasks. The thymus produces an army of T cells, which identify invading pathogens, such as bacteria and viruses, and attack and destroy them. There are millions of different T cells, each designed to recognise a specific pathogen, but there is a risk that one type might mistakenly identify one of the body's own cells or proteins.



Ordinarily, the thymus will regulate the T cells and delete those that pose the greatest risk of attacking the body's own cells and proteins. However, the researchers believe that in people who carry the variant, a lack of vitamin D during early life might impair the ability of the thymus to delete these T cells, which then go on to attack the body, leading to a loss of myelin on the nerve fibres.

"Our study implies that taking vitamin D supplements during pregnancy and the early years may reduce the risk of a child developing MS in later life," says lead author Dr Sreeram Ramagopalan. "Vitamin D is a safe and relatively cheap supplement with substantial potential health benefits. There is accumulating evidence that it can reduce the risk of developing cancer and offer protection from other autoimmune diseases."

The research has been welcomed by Simon Gillespie, Chief Executive of the MS Society (UK).

"These remarkable results tie together leading theories about the environment, genes and MS but they are only part of the jigsaw," says Mr Gillespie. "This discovery opens up new avenues of MS research and future experiments will help put the pieces together."

*CITATION: Ramagopalan SV, Maugeri NJ, Handunnetthi L, Lincoln MR, Orton S-M, et al. (2009) Expression of the Multiple Sclerosis-Associated MHC Class II Allele HLA-DRB1\*1501 Is Regulated by Vitamin D. PLoS Genet 5(2): e1000369. doi:10.1371/journal.pgen.1000369*

<http://www.plosgenetics.org/article/info:doi/10.1371/journal.pgen.1000369>

### **Single factor converts adult stem cells into embryonic-like stem cells**

The simple recipe scientists earlier discovered for making adult stem cells behave like embryonic-like stem cells just got even simpler. A new report in the February 6th issue of the journal *Cell*, a Cell Press publication, shows for the first time that neural stem cells taken from adult mice can take on the characteristics of embryonic stem cells with the addition of a single transcription factor. Transcription factors are genes that control the activity of other genes.

The discovery follows a 2006 report also in the journal *Cell* that showed that the introduction of four ingredients could transform differentiated cells taken from adult mice into "induced pluripotent stem cells" (iPS) with the physical, growth, and genetic characteristics typical of embryonic stem cells ([http://www.eurekalert.org/pub\\_releases/2006-08/cp-wff080906.php](http://www.eurekalert.org/pub_releases/2006-08/cp-wff080906.php)). Pluripotent refers to the ability to differentiate into most other cell types. The same recipe was later shown to work with human skin cells as well ([http://www.eurekalert.org/pub\\_releases/2007-11/cp-srt111307.php](http://www.eurekalert.org/pub_releases/2007-11/cp-srt111307.php)). Subsequent studies found that the four-ingredient recipe could in some cases be pared down to just two or three essential ingredients, said Hans Schöler of the Max Planck Institute for Molecular Biomedicine in Germany. "Now we've come down to just one that is sufficient. In terms of the biology, it's really quite amazing."

The discovery sheds light on centuries-old questions about what distinguishes the embryonic stem cells that give rise to egg and sperm from other body cells, Schöler said. It might also have implications for the use of reprogrammed stem cells for replacing cells lost to disease or injury.

Other researchers led by Shinya Yamanaka showed that adult cells could be reprogrammed by adding four factors – specifically Oct4, Sox2, Klf4, and c-Myc. Recently, Schöler and his colleagues demonstrated that Oct4 and Klf4 are sufficient to induce pluripotency in neural stem cells.

By omitting Klf4 in the new study, they have now established that Oct4 is the "driving force" behind the conversion of the neural stem cells into iPS cells. The lone transcription factor is not only essential, but it is also sufficient to make neural stem cells pluripotent.

Those cells, which Schöler's team calls "1F iPS" can differentiate into all three germ layers. Those primary germ layers in embryos eventually give rise to all the body's tissues and organs. Not only can those cells efficiently differentiate into neural stem cells, heart muscle cells, and germ cells, they show, but they are also capable of forming tumors when injected under the skin of nude mice. Those tumors, or teratomas, contain tissue representing all three germ layers. When injected into mouse embryos, the 1F iPS cells also found their way into the animals' developing organs and were able to be transmitted through the germ line to the next generation, they report.

The results show that adult stem cells can be made pluripotent without c-Myc and Klf4, both of which are "bona fide" oncogenes that can help turn normal cells into cancer cells, Schöler said. Limiting the number of factors is also a bonus because it means fewer genes must be inserted into the genome, where they can potentially have detrimental effects.

"Strikingly, Oct4 alone is sufficient to induce pluripotency in neural stem cells, which demonstrates its crucial role in the process of reprogramming..." the researchers concluded. "Future studies will show whether other sources of neural stem or progenitor cell populations such as mouse or human bone marrow-derived mesenchymal stem cells or dental pulp can be reprogrammed to iPS cells and whether expression of Oct4 can be induced by non-retroviral means, a prerequisite for the generation of iPS cells of therapeutic value."

*The researchers include Jeong Beom Kim, Max Planck Institute for Molecular Biomedicine, Munster, Germany; Vittorio Sebastiano, Max Planck Institute for Molecular Biomedicine, Munster, Germany; Guangming Wu, Max Planck Institute for Molecular Biomedicine, Munster, Germany; Marcos J. Arauzo-Bravo, Max Planck Institute for Molecular Biomedicine, Munster, Germany; Philipp Sasse, University of Bonn, Bonn, Germany; Luca Gentile, Max Planck Institute for Molecular Biomedicine, Munster, Germany; Kinarm Ko, Max Planck Institute for Molecular Biomedicine, Munster, Germany; David Ruau, RWTH Aachen University Medical School, Aachen, Germany; Mathias Ehrich, SEQUENOM Inc., San Diego, CA; Dirk van den Boom, SEQUENOM Inc., San Diego, CA; Johann Meyer, Hannover Medical School, Hannover, Germany; Karin Hubner, Max Planck Institute for Molecular Biomedicine, Munster, Germany; Christof Bernemann, Max Planck Institute for Molecular Biomedicine, Munster, Germany; Claudia Ortmeier, Max Planck Institute for Molecular Biomedicine, Munster, Germany; Martin Zenke, RWTH Aachen University Medical School, Aachen, Germany; Bernd K. Fleischmann, University of Bonn, Bonn, Germany; Holm Zaehres, Max Planck Institute for Molecular Biomedicine, Munster, Germany; and Hans R. Scholer, Max Planck Institute for Molecular Biomedicine, Munster, Germany.*

### **Pharmaceuticals sold in Sweden cause serious environmental harm in India**

Many of the substances in our most common medicines are manufactured in India and China. Some of these factories release large quantities of antibiotics and other pharmaceutical substances to the environment. There is an obvious risk of these releases leading to resistant bacteria.

Research from the Sahlgrenska Academy at University of Gothenburg, Sweden, shows that Sweden is a major consumer of pharmaceutical substances from factories that fail to adequately treat their wastewater. As it is difficult to find out where the pharmaceutical substances are manufactured and how much is released, it is impossible at present for consumers to avoid contributing to this environmental harm.

These findings are presented in the medical journal *Regulatory Toxicology and Pharmacology* and are highlighted today in a news article in *Nature*. Last week the research of the Swedish group became headline news in *New York Times*, *Washington Post* and *Times of India*.

"We used to think that pharmaceuticals that ended up in the environment mostly came from the use of the medicines and that the substances were dispersed through wastewater. We now know that certain factories that manufacture substances release very large quantities of active substances," says associate professor Joakim Larsson of the Sahlgrenska Academy in Gothenburg, Sweden, one of the research scientists behind the studies.

#### **The water from the pharmaceutical industries is highly toxic**

Joakim Larsson has visited the industrial zone near Hyderabad, India, an important centre for the manufacturing of pharmaceutical substances. Here his research team has taken samples of the water discharged from a treatment plant that treats wastewater from around 90 pharmaceutical factories before it is released.

"We have previously shown that the "treated" water contained exceptionally high levels of various pharmaceutical substances, including several broad-spectrum antibiotics. We estimated that the treatment plant released 45 kilograms of the antibiotic ciprofloxacin in one day, which is equivalent to five times the daily consumption of Sweden," says Larsson.

Such high levels of antibiotics in the water are a cause for alarm as there is an increased risk of spawning resistant bacteria, an issue of global concern. This can lead to those antibiotics that are invaluable today becoming ineffective sooner and not killing the bacteria of tomorrow. In addition, the environment is affected locally by the pollution; In another study by Larsson's team, published this week in *Environmental Toxicology and Chemistry*, they show that effluent diluted as much as 500 times strongly inhibit the growth of frog tadpoles.

#### **The substances manufactured in Hyderabad are sold in Sweden**

Where the active substance in a pharmaceutical product is manufactured is not public information, but the Swedish Medical Products Agency can grant exemptions for research purposes. The researchers analyzed data from the Medical Products Agency for all 242 products on the Swedish market that contained any of nine specific substances\*. They found that 123 products contained substances from India and for 74 of the products, 31 per cent, the active substance was manufactured by one of the factories that send their wastewater to the treatment plant outside Hyderabad that was studied.

"The analysis shows quite clearly that a large number of medicinal products on the Swedish market is made by manufacturers that send their effluent to a treatment plant that does not treat their water satisfactorily," says Larsson.

#### **We bear part of the responsibility**

"Sweden, which is reputed to have some of the strictest environmental legislation in the world, like other western countries therefore bears a shared responsibility for the environmental problems the medicines we consume cause in India, for example," says Larsson.

But it is impossible for the individual consumer to know today whether a substance in a medicine he or she needs to take may have caused environmental problems in manufacturing.

"It is therefore important that the production chain is made transparent. If consumers are given an opportunity to choose pharmaceutical products they know to be produced in an environmentally friendly way, this could encourage manufacturers to become more environmentally friendly," says Larsson.

\* *The selected substances were: cetirizine, ciprofloxacin, citalopram, levofloxacin, losartan, metoprolol, norfloxacin, ofloxacin and ranitidine*

### Constant compressions critical to CPR

Interrupting chest compressions during resuscitation reduces the chances of heartbeat return after defibrillation. New research published in the open access journal BMC Medicine shows that for every second of a pause in compressions there is a 1% reduction in the likelihood of success.

Kenneth Gundersen from the University of Stavanger, Norway, worked with a team of researchers to quantify the effect of compression interruptions on the probability of a return of spontaneous circulation (ROSC). He said, "We analysed data from 911 interruptions and found that every second without the blood perfusion generated by chest compressions has a negative impact on the estimated probability of ROSC". The American Heart Association's first aid guidelines were updated last year, suggesting that the 'mouth-to-mouth' component of CPR was unnecessary. This new research supports that position, in that the pause in compressions required to perform artificial respiration may reduce the patient's chances of recovering their heartbeat.

Gundersen said, "The first priority when witnessing a cardiac arrest is to make an emergency call. Beyond this our results show that performing powerful chest compressions with minimal interruptions is of utmost importance. The quality of CPR matters and everyone should practice their CPR skills at regular intervals."

*Notes to Editors:*

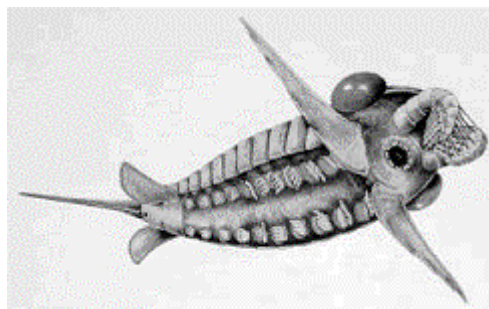
1. *Development of the probability of return of spontaneous circulation in intervals without chest compressions during out-of-hospital cardiac arrest: an observational study*

*Kenneth Gundersen, Jan Terje Kvaløy, Jo Kramer-Johansen, Petter Andreas Steen and Trygve Eftestøl  
BMC Medicine (in press)*

### Origin of claws seen in 390-million-year-old fossil

New Haven, Conn. — A missing link in the evolution of the front claw of living scorpions and horseshoe crabs was identified with the discovery of a 390 million-year-old fossil by researchers at Yale and the University of Bonn, Germany.

The specimen, named *Schinderhannes bartelsi*, was found fossilized in slate from a quarry near Bundenbach in Germany, a site that yields spectacularly durable pyrite-preserved fossils — findings collectively known as the Hunsrück Slate. The Hunsrück Slate has previously produced some of the most valuable clues to understanding the evolution of arthropods — including early shrimp-like forms, a scorpion and sea spiders as well as the ancient arthropods trilobites.



*Here is a reconstruction of Schinderhannes bartelsi. Elke Groening*

"With a head like the giant Cambrian aquatic predator *Anomalocaris* and a body like a modern arthropod, the specimen is the only known example of this unusual creature," said Derek Briggs, director of Yale's Peabody Museum of Natural History and an author of the paper appearing in the journal *Science*.

Scientists have puzzled over the origins of the paired grasping appendages found on the heads of scorpions and horseshoe crabs. The researchers suggest that *Schinderhannes* gives a hint. Their appendages may be an equivalent to those found in the ancient predatory ancestor, *Anomalocaris* — even though creatures with those head structures were thought to have become extinct by the middle of the Cambrian Period, 100 million years before *Schinderhannes* lived.

The fossil's head section has large bulbous eyes, a circular mouth opening and a pair of segmented, opposable appendages with spines projecting inward along their length. The trunk section is made up of 12 segments, each with small appendages, and a long tail spine. Between the head and trunk, there is a pair of large triangular wing-like limbs — that likely propelled the creature like a swimming penguin, according to Briggs. Unlike its ancestors from the Cambrian period, which reached three feet in length, *Schinderhannes* is only about 4 inches long.



*This is a photograph of Schinderhannes bartelsi. Steinmann Institute/University of Bonn*

This finding caps almost 20 years of study by Briggs on the Hunsrück Slate. "Sadly, the quarry from which this fabulous material comes has closed for economic reasons, so the only additional specimens that are going to appear now are items that are already in collectors' hands and that may not have been fully prepared or realized for what they are," said Briggs.

*Other authors of the paper are Gabriele Kühn and Jes Rust at the University of Bonn, Germany. Funding for the research was from the German Science Foundation and the Humboldt Foundation. Background information on Anomalocaris and the Hunsrück Slate are available online.*

*Citation: Science (February 6, 2009)*

### Why teenagers can't see your point of view

\* 11:29 05 February 2009 by Ewen Callaway

Teenagers might have a new excuse for ignoring their parent's orders. Their brain's ability to adopt the viewpoint of others is still budding, new research suggests.

Known as theory of mind, the ability to infer another's perspective – emotional, intellectual, or visual – improves with age. Studies of infants, toddlers and children have documented gradual improvement in this skill with age.

In a typical test, kids watch two puppets – Sally and Anne – play with a marble, then put the marble back in a box. Anne "leaves" and Sally grabs the marble, plays with it, and then returns the marble instead to a bag.

Where will Anne first search for the marble, researchers ask the children.

"Before four, kids say she's going to look in the bag, but after four they know she has a false belief," says Iroise Dumontheil, a cognitive neuroscientist at University College London, UK, who led the new study.

However, brain scans suggest that a teenage mind toils harder when inferring the outlook of others, compared with adults. And a brain region implicated in theory of mind, the medial prefrontal cortex, continues to develop through adolescence, Dumontheil says.

#### Varied viewpoint

To see if there is a behavioural consequence of these biological changes, she and colleagues tested children, adolescents, and adults on their ability to infer the spatial perspective of another person in a simple computer game.

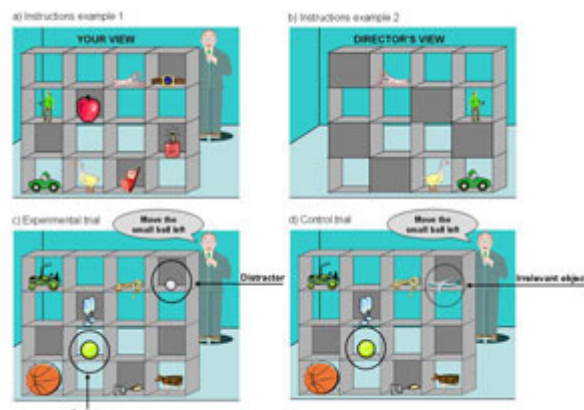
Test subjects – 179 females ranging in age from 7 to 27 – saw a bookshelf with a variety of different sized balls and other objects on four different rows. Some of the objects sit in front of opaque backgrounds, obscured to someone standing on the other side of the shelf, while some sit in front of a see-through background.

Participants are asked to adopt the perspective of a man standing on the other side of the shelf and move the small ball to the left, using a mouse. In a typical test, a golf ball and tennis ball are both visible to the participant, but the golf ball is obscured from the point of view of the observer. The correct response, then, is to move the tennis ball.

Kids under the age of 10 moved the wrong ball in about three-quarters of trials. Children aged 10 through 13 scored marginally better, and teens answered wrong on two-thirds of trials. Adults, however, did better than 50-50, on average.

*A simple computer game reveals how able volunteers are to put themselves on the shoes of others. Click the link below to see the frames in full detail (Image: Iroise Dumontheil/Developmental Science)*

[See images of the game here](#)



#### Egotistical behaviour

This, Dumontheil says, is the first behavioural evidence showing that theory of mind is still improving even through teenage years.

"You probably first need to have the idea that somebody has a different spatial perspective and then you can move onto higher thoughts," she says.

Her team plans to next test boys and men on the same task to determine if theory of mind develops differently in males than in females.

The study's findings may also explain teens' sometimes callous actions.

"What is really new and amazing about this paper, is that they show that adolescents show strong egocentric behaviour that is very similar to that of young children," says Boaz Keysar, a cognitive psychologist at the University of Chicago. *Journal reference: Developmental Science (in press)*

## Antarctic bulge could flood Washington DC

\* 19:00 05 February 2009 by David Robson

Rather than spreading out evenly across all the oceans, water from melted Antarctic ice sheets will gather around North America and the Indian Ocean. That's bad news for the US East Coast, which could bear the brunt of one of these oceanic bulges.

Many previous models of the rising sea levels due to climate change assumed that water from melted ice sheets and glaciers would simply run into the oceans and fill them uniformly. These models predict a 5-metre rise in sea levels if the West Antarctic ice sheet melts, but fail to acknowledge three important factors.

First, Jerry Mitrovica and colleagues from the University of Toronto in Canada considered the gravitational attraction of the Antarctic ice sheets on the surrounding water, which pulls it towards the South Pole. As the ice sheet melts, this bulge of water dissipates into surrounding oceans along with the meltwater. So while the sea level near Antarctica will fall, sea levels away from the South Pole will rise.

Once the ice melts, the release of pressure could also cause the Antarctic continent to rise by 100 metres. And as the weight of the ice pressing down on the continental shelf is released, the rock will spring back, displacing seawater that will also spread across the oceans.

Redistributing this mass of water could even change the axis of the Earth's spin. The team estimates that the South Pole will shift by 500 metres towards the west of Antarctica, and the North Pole will shift in the opposite direction. Since the spin of the Earth creates bulges of oceanic water in the regions between the equator and the poles, these bulges will also shift slightly with the changing axis.

### Washington awash

The upshot is that the North American continent and the Indian Ocean will experience the greatest changes in sea level - adding 1 or 2 metres to the current estimates. Washington DC sits squarely in this area, meaning it could face a 6.3-metre sea level rise in total. California will also be in the target zone.

"Policy-makers must realise that the effects could be greater or smaller in different areas," says team member Natalya Gomez. The team have so far only considered one ice sheet, so the effects of other ice sheets across the world could also have a similar impact, she says.

However, these models assume that all the West Antarctic sea ice will melt, but Peter Convey from the British Antarctic Survey in Cambridge points out this may not necessarily be the case. "It would be dangerously easy to get people to focus on the 6-metre figure, but it just might not happen like that," he says.

Jonathan Gregory from the University of Reading in the UK, who is part of the Intergovernmental Panel on Climate Change, however, thinks the work should be helpful once this has been reliably evaluated.

*Journal reference: Science: DOI: 10.1126/science.1166510*

## Parasitic butterflies dupe hosts with ant music

\* 19:00 05 February 2009 by Ewen Callaway

Though they wouldn't win much applause at a karaoke lounge, the infant forms of blue butterflies can belt out a convincing cover version of a tune favoured by red ants - which show their appreciation by protecting and feeding the butterfly larvae.

Researchers have found that the larvae and pupae of *Maculinea rebeli* - a parasitic butterfly native to western Europe, though threatened with extinction - impersonate red ants so faithfully that worker ants worship them as if they were queens, caring for the developing caterpillar even at the expense of their own lives.

"They appeared to be treating the caterpillars as if they were the holiest of holiest, the pinnacle of power, the queen ant," says Jeremy Thomas, an entomologist at the University of Oxford who led the new study.



*Caterpillar inside a red ant nest, being fed regurgitations by a worker ant (Courtesy of Jeremy Thomas)*

*Listen to caterpillars imitating ants [here](#), pupae making ant-noises [here](#), the noise of the queen ant [here](#) and a worker ant [here](#)*

### Playing queen

As young caterpillars, *M. rebeli* spend their days gorging on leafy greens. When they're nearly ready to begin their transformation into a butterfly, the caterpillars descend to the forest floor and secrete ant-like chemicals. Duped worker ants ferry the caterpillar to its colony, where it is accepted as another ant, based on its smell alone.

But Thomas noticed that the interlopers seem to get particularly special treatment. When he disturbed a laboratory colony, workers sacrificed their own kin to save the butterfly larvae - much as they would if a queen

ant were threatened. "There must be some form of communication by the butterflies that make the ants think they're royal, and at the same time we were pretty damn sure they weren't by chemicals," he says.

Puzzled, his team wondered whether a mysterious ticking sound emitted by blue butterfly larvae and pupae could explain this privileged treatment. The ants produce a song of their own, with subtle differences between queen and worker.

Using miniature microphones hooked up to an MP3 recorder, Thomas' team captured the tunes made by queen and worker ants, as well as by the butterfly larvae and pupae. Auditory analysis showed similarities in key acoustic features of the ant and butterfly sounds, such as resonant frequency.

### **Ant attraction**

The researchers then used Lilliputian speakers to audition the various songs to workers. When they listened to their own songs, the workers perked up. "Instead of running away or acting with aggression, the speakers attracted the worker ants to them and they tapped them with their antennae with great interest," says Thomas.

The recording of a queen's song inspired even more interest. Workers surrounded the speaker and refused to budge. Amazingly, Thomas' team observed nearly the same behaviour when they played the butterfly songs to the ants - suggesting that auditory mimicry is the key to the butterflies' ascendancy.

"This use of sound potentially solves the mystery of how they mimic the queen even though they don't smell like the queen," says David Nash, an entomologist at the University of Copenhagen. "In hindsight, the results are so consistent and logical," agrees Josef Settele, at the Helmholtz Centre for Environmental Research in Halle, Germany.

Other species of blue butterfly use sound to foster a more equitable relationship with ants, and parasitic ants probably adapted these tunes for their own nefarious purposes, Thomas theorises. But why haven't the ants evolved new chemicals and sounds, rendering them indifferent to the imposters' smells and songs?

Researchers previously assumed that ants have little incentive to do this, because butterflies plague only a small proportion of ant colonies. But Nash's lab recently found that a related species of ant has done just that with its chemicals. No evidence yet exists for sound wars, but Thomas will be on the lookout.

"There may well be an arms race going on," he says. *Journal reference: Science, DOI: 10.1126/science.1163583*

## **F.D.A. Approves Drug From Gene-Altered Goats**

**By ANDREW POLLACK**

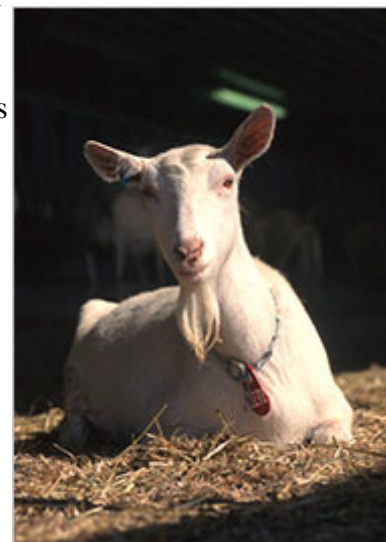
Opening the barn door to a new era in farming and pharmaceuticals, the Food and Drug Administration on Friday approved the first drug produced by livestock that have been given a human gene.

The drug, meant to prevent fatal blood clots in people with a rare condition, is a human protein extracted from the milk of genetically engineered goats.

At the same time, the F.D.A. also approved the goats used to make the drug, the first such animals cleared under guidelines the agency adopted only last month to regulate the use of transgenic animals in the nation's drug and food supply.

Made by a company called GTC Biotherapeutics, the human anticlotting protein is produced by a herd of 200 bioengineered goats living under carefully controlled conditions on a farm in central Massachusetts.

Proponents say such "pharm animals" could become a means of producing biotechnology drugs at lower cost or in greater quantities than the existing methods — which include extracting proteins from donated human blood or growing them in large steel vats of genetically engineered cells.



*A goat at GTC Biotherapeutics' farm. GTC Biotherapeutics*

The protein in the goat milk, antithrombin, is sometimes in short supply or unavailable for pharmaceutical use because of a shortage of human plasma donations. GTC Biotherapeutics said one of its goats can produce as much antithrombin in a year as can be derived from 90,000 blood donations. And if more drug is needed, the herd can be expanded.

"If you need more, you breed more," said Thomas Newberry, a spokesman for GTC, which is based in Framingham, Mass.

Drugs have been derived from animals before, of course. Most insulin used by people with diabetes formerly came from pigs or cows. Genetically engineered mice are now used to develop some drug ingredients. But this is the first drug from a herd of genetically engineered animals created specifically to serve as living pharmaceutical factories.

Turning animals into walking drug producers does not sit well with some environmental advocates and animal rights activists.

“It is a mechanistic use of animals that seems to perpetuate the notion of their being merely tools for human use rather than sentient creatures,” the Humane Society of the United States says in its position paper on the practice.

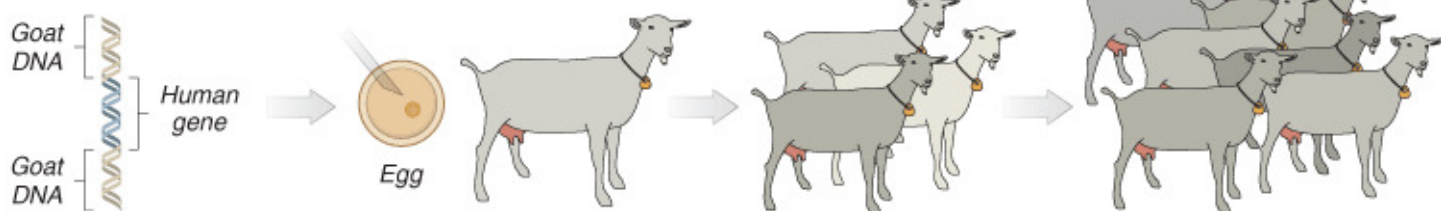
There are other concerns: that the animals could be harmed, that animal germs might contaminate the drug, that the milk or meat from genetically engineered drug-producing animals might enter the food supply or that the animals might escape and breed with others, spreading the gene, with unpredictable consequences.

But the F.D.A. approval could now encourage drug makers to consider this type of production.

The F.D.A.’s move “really takes away one of the biggest issues that have always been on the table, which is

## Bioengineering on the Farm

The Food and Drug Administration has approved the first drug produced in the milk of genetically engineered animals.



### MODIFYING THE DNA

A human gene that produces the blood protein antithrombin is inserted into a short strand of goat DNA.

### IMPLANTING THE DNA

The modified DNA is injected into the nucleus of a fertilized goat egg, which is then implanted into a female.

### TESTING THE OFFSPRING

Kids born from the modified eggs are tested for the presence of antithrombin in their milk. Promising kids are bred normally to create a herd of modified goats.

### EXTRACTING THE PROTEIN

Milk from the herd is filtered and purified. Annually, each goat can produce as much antithrombin as 90,000 human blood donations.

Sources: GTC Biotherapeutics

how do regulatory agencies view this kind of technology,” said Samir Singh, president of the American operations of Pharming, another company using such technology.

Pharming, which is based in the Netherlands, plans to apply this year for approval of a drug, produced in the milk of transgenic rabbits, to treat hereditary angioedema, a protein deficiency that can lead to dangerous swelling of tissues.

Another company, PharmAthene, is developing a treatment for nerve gas poisoning in the milk of transgenic goats.

Still, it could be difficult to persuade established manufacturers to depart from their existing methods, which have improved markedly since GTC first began its work.

“I think we have very good ways of making therapeutic proteins today,” said Norbert Riedel, chief scientific officer at Baxter International, which makes proteins both from human plasma and in cell cultures grown in huge steel tanks.

Sales of the GTC drug, called ATryn, are expected to be modest, judging from the small sales so far in Europe, where the drug was approved in 2006.

ATryn will be sold in the United States by Ovation Pharmaceuticals, which said it had not yet set the price.

GTC’s stock, which was below 11 cents in mid-December, had risen recently on expectation of the F.D.A. approval. It traded above 90 cents a share earlier this week. On Friday, as investors evidently sold on the news, it fell more than 14 percent, closing at 70 cents.

The drug was approved to prevent blood clots in people born with a rare hereditary deficiency of antithrombin while they undergo surgery or childbirth. At other times such people can reduce their clotting risks by taking blood thinners like warfarin, but during surgery or childbirth blood thinners are typically avoided because of the risk of excessive bleeding.

To make its protein, GTC took the human gene for antithrombin and linked it to goat DNA that normally controls production of a protein found in milk. That ensured that the antithrombin would be produced only in the milk.

The gene was injected into a one-celled goat embryo, which was then implanted into the womb of a surrogate mother. After a goat was born that produced the protein in its milk, the herd was expanded by conventional breeding.

Many of the newer protein-based drugs, like the cancer drug Avastin and the arthritis drug Enbrel, are produced in genetically engineered Chinese hamster ovary cells that are grown in big stainless steel vats. But a cell culture factory can cost hundreds of millions of dollars to build. Using livestock shrinks the investment to tens of millions of dollars, said Geoffrey Cox, GTC's chief executive.

GTC executives say the animal technology might be best suited to making proteins that cannot be produced well in cell cultures. Antithrombin, the protein in ATryn, is one such drug. Some other drugs require huge volumes that are impractical to achieve with cells.

Production in animal milk might also appeal to new companies hoping to make lower-priced copycat versions of biotechnology drugs, if the regulatory procedures are eventually adopted for approving generic versions of such drugs.

GTC itself is planning to make a copycat version of Rituxan, a cancer and arthritis drug sold by Biogen Idec and Genentech. It is also planning to make clotting factors for hemophilia treatment.

One risk of using animals is that drug production can be lost if a disease wipes out the herd. Mr. Newberry, the GTC spokesman, said the goats were fully vaccinated. Access to them by people is controlled and there is a double fence around the farm to keep out wildlife.

Mr. Newberry said that none of the goats in the herd, including nontransgenic ones used as surrogate mothers, would be allowed in the food supply. Nor will any of the milk.

The F.D.A. said it was confident that products from the goats would not enter the food supply or harm the environment. "There were no novel or controversial issues" with the goats, Bernadette Dunham, director of the agency's Center for Veterinary Medicine, said Friday.

But Gregory Jaffe of the Center for Science in the Public Interest, a Washington consumer group, called for assurances that the milk or meat would be safe if it did inadvertently enter the food supply.

"Humans are fallible; accidents happen," he said.

### **Number of alien worlds quantified**

Intelligent civilisations are out there and there could be thousands of them, according to an Edinburgh scientist.

The discovery of more than 330 planets outside our solar system in recent years has helped refine the number of life forms that are likely to exist.

The current research estimates that there are at least 361 intelligent civilisations in our Galaxy and possibly as many as 38,000.

The work is reported in the International Journal of Astrobiology.

Even with the higher of the two estimates, however, it is not very likely that contact could be established with alien worlds.

While researchers often come up with overall estimates of the likelihood of intelligent life in the universe, it is a process fraught with guesswork; recent guesses put the number anywhere between a million and less than one.

"It's a process of quantifying our ignorance," said Duncan Forgan, the University of Edinburgh researcher who carried out the work.

In his new approach, Mr Forgan simulated a galaxy much like our own, allowing it to develop solar systems based on what is now known from the existence of so-called exoplanets in our galactic neighbourhood.

These simulated alien worlds were then subjected to a number of different scenarios.

The first assumed that it is difficult for life to be formed but easy for it to evolve, and suggested there were 361 intelligent civilisations in the galaxy.

A second scenario assumed life was easily formed but struggled to develop intelligence. Under these conditions, 31,513 other forms of life were estimated to exist.

The final scenario examined the possibility that life could be passed from one planet to another during asteroid collisions - a popular theory for how life arose here on Earth.

That approach gave a result of some 37,964 intelligent civilisations in existence.

### **Form and function**

While far-flung planets may reduce uncertainty in how many Earth-like planets there are, some variables in the estimate will remain guesses.



For example, the time from a planet's formation to the first sparks of life, or from there to the first intelligent civilisations, are large variables in the overall estimate.

For those, Mr Forgan says, we will have to continue to assume Earth is an average case.

"It is important to realise that the picture we've built up is still incomplete," said Mr. Forgan.

"Even if alien life forms do exist, we may not necessarily be able to make contact with them, and we have no idea what form they would take.

"Life on other planets may be as varied as life on Earth and we cannot predict what intelligent life on other planets would look like or how they might behave."

### **Photosynthesis viewed in a flash**

**By Jason Palmer** Science and technology reporter, BBC News

A new method of examining the inner workings of plants has shed light on how they harvest the Sun's energy.

Researchers have taken laser snapshots lasting just one ten-thousandth of a billionth of a second to examine the role of electrons in energy transfer.

The approach will be key in discovering how energy trickles through other systems, such as electronic devices, and could lead to better solar cells.

The work is published in the current issue of Physical Review Letters.

Ian Mercer of University College Dublin, Ireland, collaborating with researchers at Imperial College London, UK, examined the protein LH2, a well-known photosynthetic system.

The protein helps to pull electrons out of water which are then used to drive the reaction that makes sugars from carbon dioxide.

"More generally, we're trying to understand how nature can transport energy across large molecules, and photosynthesis is a good example of where nature does it remarkably efficiently," Dr Mercer told BBC News.

Significant research has been performed to assess the role of electrons in that process with a view to increasing the performance of solar cells, most of which currently operate at an efficiency around just 10%.

#### **Colour full**

What has remained unclear, though, is the degree to which electrons interact with each other or with other molecules of the machinery.

A number of laser-based methods have been developed to examine that electron coupling, but they require that the delicate proteins are subject to thousands or millions of laser pulses, which can change their structure or destroy them altogether.

Dr Mercer's method can look at those electron couplings directly with just one "ultrafast" laser pulse lasting 100 femtoseconds - or ten thousand million times shorter than an average camera flash.

Such short pulses are made up of a broad spectrum of colours, with each colour corresponding to the particular energy of the photons that make it.

The new method works by splitting powerful laser pulses into three beams and crossing them in the protein samples in a specific geometry.

The light that comes out gives for the first time an unambiguous picture of how the different colours - and thus energies - interact inside the protein.

"The fact that it's instantaneous is not just a detail, not just a nicety," Dr Mercer said. "It means we're able to take a picture of any system before that molecule has had a chance for its atoms to move significantly.

"We're looking at the shape of something before the laser was even there - it's a whole new world of what you can look at."

#### **Wide application**

The new method is applicable across a wide array of samples; the intricate details of electron transport are the subject of study in disciplines ranging from electronics to drug design.

The results could be used to help mimic that process in the design of more efficient solar cells - a pursuit in which Dr Mercer says "the impact of a small increase in efficiency is very large for the world".

The method was only made possible by developments at Imperial College London in lasers that can provide the huge range of colours in the laser pulses, a pursuit headed up by John Tisch.

"The laser source has opened up a new frontier of optics," Dr Tisch said.

"The beauty of it is that you really can extract the information in a single shot - the data was coming out of this much faster than it could be viewed."

Dr Mercer said that the team is now in discussion with a number of researchers who are keen to apply the method in their own work.

"There isn't a conversation I've had that hasn't resulted in someone saying, 'well, let's get a sample in there!'"

## **A Natural, Alternative Insect Repellent to DEET**

Isolongifolenone found as effective as DEET against mosquitoes and ticks

Lanham, MD; February 5, 2009 – Isolongifolenone, a natural compound found in the Tauroniro tree (*Humiria balsamifera*) of South America, has been found to effectively deter biting of mosquitoes and to repel ticks, both of which are known spreaders of diseases such as malaria, West Nile virus, and Lyme disease.

Derivatives of isolongifolenone have been widely and safely used as fragrances in cosmetics, perfumes, deodorants, and paper products, and new processing methods may make it as cheap to produce as DEET.

The results of this research are presented in the latest issue of *Journal of Medical Entomology* in an article by Aijun Zhang et. al titled "Isolongifolenone: A Novel Sesquiterpene Repellent of Ticks and Mosquitoes."

The authors found that isolongifolenone deters the biting of the mosquitoes *Aedes aegypti* (L.) and *Anopheles stephensi* Liston more effectively than the widely used synthetic chemical repellent N,N-diethyl-3-methyl benzamide (DEET) in laboratory bioassays. Furthermore, it repelled blacklegged ticks and lone star ticks as effectively as DEET.

Since "isolongifolenone is easily synthesized from inexpensive turpentine oil feedstock," the authors write, "we are therefore confident that the compound has significant potential as an inexpensive and safe repellent for protection of large human populations against blood-feeding arthropods."

In addition, a new, patented method developed by the authors to efficiently produce isolongifolenone would make it even more cost effective. *Full text of the article is available at <http://www.entsoc.org/iso.htm>.*

## **New paper offers key insights into how new species emerge**

This year marks both the bicentennial of Charles Darwin's birth and the 150th anniversary of the publication of his seminal work "On the Origin of Species." Just in time for the Darwin observances, a new paper appearing today in the journal *Science* by a team led by University of Notre Dame researchers Andrew Forbes, Thomas Powell, and Jeffrey Feder offers important insights into how new species come to be.

"This study is important because it shows how biodiversity itself can be a major generator of biodiversity," Feder said. "As new species form, they can create new opportunities for others to take advantage of, which, in turn, can lead to a chain reaction of ever more new species."

In the paper, Forbes, Powell, Feder and colleagues demonstrate that the parasitic wasp *Diachasma alloeum* is evolving into a new incipient species as a result of specializing on the *Rhagoletis* fruit flies that they attack. These *Rhagoletis* flies are themselves actively diversifying and forming new species.

For the flies, the process begins with a shift to a new host plant. *Rhagoletis pomonella* flies originally attacked the fruit of hawthorn trees. But about 150 years ago, a portion of the hawthorn fly population shifted and began to feed on apples. In ecologically adapting to apples as a new host plant, apple flies are becoming genetically distinct and reproductively isolated from hawthorn flies. The apple race of *Rhagoletis* flies is now a major pest of apples in the United States and is the proverbial "worm in the apple."

Every new opportunity opens a world for others, however. The Notre Dame researchers show that the *Diachasma* wasp that parasitizes *Rhagoletis* has also shifted to use the fly larvae that feed within the apple as a new food resource. Indeed, the wasp has evolved many of the same types of ecological adaptations to live on flies in apples that the apple fly evolved before it.

And so it goes, with the formation of one new species planting the seed that germinates in the beginning of another.

But in a plot twist, the apple wasp's ancestors appear to have come from a *Rhagoletis* fly infesting blueberries rather than hawthorns — one turn does not always lead directly to another.

"The idea that there are 'speciation cascades' operating in nature has important applications not only for understanding the process of speciation, but also for theories concerning how biodiversity reforms following mass extinction events, for why certain groups of organisms with certain lifestyles may be more diverse than others, and for why certain areas of biotic regions may have more life forms than others," Feder said.

Where Darwin once traveled to the Galapagos Islands and sleuthed to other far-flung places in pursuit of the origins of species, the research on the apple fly and the apple wasp reveals that important clues to solving his ultimate "mystery of mysteries" can be found all around us, happening right before our eyes in our own back yards.

*Other researchers participating in the study are Lukasz L. Stelinski from the University of Florida and James J. Smith from Michigan State University.*

## Oldest Human Hair Found in Hyena Poop Fossil?

Charles Q. Choi for National Geographic News February 6, 2009

The oldest known human hairs could be the strands discovered in fossil hyena poop found in a South African cave, a new study hints. Researchers discovered the rock-hard hyena dung near the Sterkfontein caves, where many early human ancestor fossils have been found. Each white, round fossil turd, or coprolite, is roughly 0.8 inch (2 centimeters) across. They were found embedded in sediments 195,000 to 257,000 years old.

Until now, the oldest known human hair was from a 9,000-year-old Chilean mummy.

The sizes and shapes of the coprolites and their location suggest they came from brown hyenas, which still live in the region's caves today.

It's not clear which species the newfound human hairs are from, since the human fossil record for this time span is exceedingly limited, the researchers say. But the hairs' age "covers just before when we think modern humans emerged, and overlaps with the existence and end of *Homo heidelbergensis*," said study co-author Lucinda Backwell, a paleoanthropologist at the University of the Witwatersrand in Johannesburg, South Africa.

"The hairs could belong to either of them, or of course to [a species] not yet recognized," added Backwell, whose findings appeared online January 31 in the *Journal of Archaeological Science*.

### Not King of the Hill

Backwell and her colleagues used tweezers to extract 40 fossilized hairs resembling glass needles from one of the hyena coprolites. Scanning-electron-microscope images revealed wavy bands of scales on the hairs—a pattern typical of modern primates, with human hair being the closest match.

### Buying experiences, not possessions, leads to greater happiness

Can money make us happy if we spend it on the right purchases? A new psychology study suggests that buying life experiences rather than material possessions leads to greater happiness for both the consumer and those around them. The findings will be presented at the Society for Personality and Social Psychology annual meeting on Feb. 7.

The study demonstrates that experiential purchases, such as a meal out or theater tickets, result in increased well-being because they satisfy higher order needs, specifically the need for social connectedness and vitality -- a feeling of being alive.

"These findings support an extension of basic need theory, where purchases that increase psychological need satisfaction will produce the greatest well-being," said Ryan Howell, assistant professor of psychology at San Francisco State University.

Participants in the study were asked to write reflections and answer questions about their recent purchases. Participants indicated that experiential purchases represented money better spent and greater happiness for both themselves and others. The results also indicate that experiences produce more happiness regardless of the amount spent or the income of the consumer.

Experiences also lead to longer-term satisfaction. "Purchased experiences provide memory capital," Howell said. "We don't tend to get bored of happy memories like we do with a material object.

"People still believe that more money will make them happy, even though 35 years of research has suggested the opposite," Howell said. "Maybe this belief has held because money is making some people happy some of the time, at least when they spend it on life experiences."

"The mediators of experiential purchases: Determining the impact of psychological need satisfaction" was conducted by Ryan Howell, assistant professor of psychology at San Francisco State University and SF State graduate Graham Hill.

## 1709: The year that Europe froze

\* 07 February 2009 by Stephanie Pain

*People across Europe awoke on 6 January 1709 to find the temperature had plummeted. A three-week freeze was followed by a brief thaw - and then the mercury plunged again and stayed there. From Scandinavia in the north to Italy in the south, and from Czechoslovakia in the east to the west coast of France, everything turned to ice. The sea froze. Lakes and rivers froze, and the soil froze to a depth of a metre or more. Livestock died from cold in their barns, chicken's combs froze and fell off, trees exploded and travellers froze to death on the roads. It was the coldest winter in 500 years.*

IN ENGLAND they called the winter of 1709 the Great Frost. In France it entered legend as Le Grand Hiver, three months of deadly cold that ushered in a year of famine and food riots. In Scandinavia the Baltic froze so thoroughly that people could walk across the ice as late as April. In Switzerland hungry wolves crept into villages. Venetians skidded across their frozen lagoon, while off Italy's west coast, sailors aboard English men-of-war died from the cold. "I believe the Frost was greater (if not more universal also) than any other within the

Memory of Man," wrote William Derham, one of England's most meticulous meteorological observers. He was right. Three hundred years on, it holds the record as the coldest European winter of the past half-millennium.

Derham was the Rector of Upminster, a short ride north-east of London. He had been checking his thermometer and barometer three times a day since 1697. Similarly dedicated observers scattered across Europe did much the same and their records tally remarkably closely. On the night of 5 January, the temperature fell dramatically and kept on falling. On 10 January, Derham logged  $-12^{\circ}\text{C}$ , the lowest temperature he had ever measured. In France, the temperature dipped lower still. In Paris, it sank to  $-15^{\circ}\text{C}$  on 14 January and stayed there for 11 days.

After a brief thaw at the end of that month the cold returned with a vengeance and stayed until mid-March.

*Part of a lagoon which froze over in 1708, Venice, Italy, by Gabriele Bella (1733-99) (Image: The Art Archive / Querini Stampalia Foundation Venice / Gianni Dagli Orti)*



Later that year, Derham wrote a detailed account of the freeze and the destruction it caused for the Royal Society's Transactions. Fish froze in the rivers, game lay down in the fields and died, and small birds perished by the million. The loss of tender herbs and exotic fruit trees was no surprise, but even hardy native oaks and ash trees succumbed. The loss of the wheat crop was "a general calamity". England's troubles were trifling, however, compared to the suffering across the English Channel.

In France, the freeze gripped the whole country as far as the Mediterranean. Even the king and his courtiers at the sumptuous Palace of Versailles struggled to keep warm. The Duchess of Orleans wrote to her aunt in Germany: "I am sitting by a roaring fire, have a screen before the door, which is closed, so that I can sit here with a sable fur piece around my neck and my feet in a bearskin sack and I am still shivering with cold and can barely hold the pen. Never in my life have I seen a winter such as this one."

In more humble homes, people went to bed and woke to find their nightcaps frozen to the bed-head. Bread froze so hard it took an axe to cut it. According to a canon from Beaune in Burgundy, "travellers died in the countryside, livestock in the stables, wild animals in the woods; nearly all the birds died, wine froze in barrels and public fires were lit to warm the poor". From all over the country came reports of people found frozen to death. And with roads and rivers blocked by snow and ice, it was impossible to transport food to the cities. Paris waited three months for fresh supplies.

There was worse to come. Everywhere, fruit, nut and olive trees died. The winter wheat crop was destroyed. When spring finally arrived, the cold was replaced by worsening food shortages. In Paris, many survived only because the authorities, fearing an uprising, forced the rich to provide soup kitchens. With no grain to make bread, some country people made "flour" by grinding ferns, bulking out their loaves with nettles and thistles. By the summer, there were reports of starving people in the fields "eating grass like sheep". Before the year was out more than a million had died from cold or starvation.

The fact that so many people left accounts of the freeze suggests the winter of 1708/1709 was unusually bad, but just how extraordinary was it?

In 2004, Jürg Luterbacher, a climatologist at the University of Bern in Switzerland, produced a month-by-month reconstruction of Europe's climate since 1500, using a combination of direct measurements, proxy indicators of temperature such as tree rings and ice cores, and data gleaned from historical documents (Science, vol 303, p 1499). The winter of 1708-1709 was the coldest. Across large parts of Europe the temperature was as much as  $7^{\circ}\text{C}$  below the average for 20th-century Europe.

Why it was quite so cold is harder to explain. The Little Ice Age was at its climax and Europe was experiencing climatically turbulent times: the 1690s saw a string of cold summers and failed harvests, while the summer of 1707 was so hot people died from heat exhaustion. Overall, the climate was colder, with the sun's output at its lowest for millennia. There were some spectacular volcanic eruptions in 1707 and 1708, including Mount Fuji in Japan and Santorini and Vesuvius in Europe. These would have sent dust high into the atmosphere, forming a veil over Europe. Such dust veils normally lead to cooler summers and sometimes warmer winters, but climatologists think that during this persistent cold phase, dust may have depressed both summer and winter temperatures.

None of these things accounts for the extremity of that particular winter, however. "Something unusual seems to have been happening," says Dennis Wheeler, a climatologist at the University of Sunderland, UK. As part of the European Union's Millennium Project, which aims to reconstruct the past 1000 years of Europe's climate, Wheeler is extracting data from Royal Navy logbooks, which provide daily observations of wind and weather. "With daily data you can produce very reliable monthly averages but you can also see what happened from one day to the next," says Wheeler. He and his colleagues have now compiled a database of daily observations stretching back to 1685 from the English Channel area. "This is a key climatic zone. The weather there reflects wider conditions across the Atlantic, which is where in normal circumstances much European weather originates."

The most immediate cause of cold winters in Europe is usually an icy wind from Siberia. "What you would expect would be long runs of easterly winds with a well-developed anticyclone over Scandinavia sucking in cold air from Siberia," says Wheeler. Instead, his data show a predominance of southerly and westerly winds - which would normally bring warm air to Europe. "There were only occasional northerlies and easterlies and those were never for more than a few days," says Wheeler. Another odd finding was that January was unusually stormy. Winter storms tend to bring milder, if wilder, weather to Europe. "This combination of cold, storms and westerlies suggests some other mechanism was responsible for that winter."

There may be no easy explanation for the Great Frost of 1709, but unexpected weather patterns revealed by Wheeler's data underline why climate reconstructions are so important. "We need to explain the natural variation in climate over past centuries so that we can tease apart all those factors that contribute to climate change. But before we can do that we need to nail down those changes in detail," says Wheeler. "Climate doesn't behave consistently and warmer and colder, drier and wetter periods can't always be explained by the same mechanisms." In the two decades after that terrible winter, the climate warmed very rapidly. "Some people point to that and say today's warming is nothing new. But they are not comparable. The factors causing warming then were quite different from those operating now."

### ***New guideline for prescribing opioid pain drugs published***

#### ***Researchers at Oregon Health & Science University provide evidence to support first published guideline for treating chronic non-cancer pain with opioid medications***

A national panel of pain management experts representing the American Pain Society (APS) and the American Academy of Pain Medicine (AAPM) has published the first comprehensive, evidence-based clinical practice guideline to assist clinicians in prescribing potent opioid pain medications for patients with chronic non-cancer pain. The long-awaited guideline appears in the current issue of *The Journal of Pain*, [www.jpain.org](http://www.jpain.org).

To create this guideline, researchers in the Oregon Evidence-based Practice Center (EPC) at Oregon Health & Science University collaborated with the APS and AAPM for two years, reviewing more than 8,000 published abstracts and nonpublished studies to assess clinical evidence on which the new recommendations are based.

"This guideline was a true multidisciplinary effort that sought to address in a balanced manner the many challenging issues that clinicians face with regard to when and how to prescribe opioids for chronic noncancer pain," said Roger Chou, M.D., principal investigator; director of the American Pain Society Clinical Practice Guidelines Program; scientific director of the Oregon Evidence-Based Practice Center at OHSU; and associate professor of medical informatics and clinical epidemiology, and medicine (general internal medicine and geriatrics) in the OHSU School of Medicine.

"A key part of this process was performing a comprehensive literature review to inform the recommendations - though an important take-home message is that even though the recommendations represent the best judgment of the panel based on the currently available literature, there is still a lot of research that needs to be done."

The expert panel concluded that opioid pain medications are safe and effective for carefully selected, well-monitored patients with chronic non-cancer pain. They made 25 specific recommendations and achieved unanimous consensus on nearly all.

Opioid prescribing has increased significantly due to growing professional acceptance that the drugs can relieve chronic non-cancer pain, and the guideline acknowledges there are widespread concerns about increases in prescription opioid abuse, addiction and diversion.

Opioids, such as morphine, oxycodone, oxymorphone and fentanyl are potent analgesics. They traditionally have been used to relieve pain following surgery, from cancer and at the end of life. Today opioids are used widely to relieve severe pain caused by chronic low-back injury, accident trauma, crippling arthritis, sickle cell, fibromyalgia, and other painful conditions.

Prior to initiating chronic opioid therapy, the guideline advises clinicians to determine if the pain can be treated with other medications. If opioids are appropriate, the clinician should conduct a thorough medical history and examination and assess potential risk for substance abuse, misuse or addiction.

### **Diligent Patient Monitoring Is Essential**

A key recommendation urges clinicians to continuously assess patients on chronic opioid therapy by monitoring pain intensity, level of functioning and adherence to prescribed treatments. Periodic drug screens should be ordered for patients at risk for aberrant drug behavior.

Other recommendations in the APS/AAPM clinical practice guideline include:

- \* **Methadone:** Use of methadone for pain management has increased dramatically but few trials have evaluated its benefits and harms for treatment of chronic non-cancer pain. Methadone, therefore, should be started at low doses and titrated slowly. Because of its long half-life and variable pharmacokinetics, the panel recommends methadone not be used to treat breakthrough pain or as an as-needed medication.
- \* **Abusers:** Chronic opioid therapy must be discontinued in patients known to be diverting their medication or in those engaging in serious aberrant behaviors.
- \* **Breakthrough Pain:** As-needed opioids can be prescribed based on initial and ongoing analysis of therapeutic benefit versus risk.
- \* **High Doses:** Patients who need high doses of opioids (200 mg daily of morphine or equivalent) should be evaluated for adverse events on an ongoing basis, and clinicians should consider rotating pain medications when patients experience intolerable side effects or inadequate benefit despite appropriate dose increases.
- \* **Driving and Work Safety:** Patients should be educated about the greater risk for impairment when starting chronic opioid therapy and counseled not to drive or engage in potentially dangerous work if impaired.
- \* **Pregnancy:** Clinicians should counsel women about risks of opioids in pregnancy and encourage minimal or no use of chronic opioid therapy unless potential benefits outweigh risks.

The guideline on opioid therapy for chronic non-cancer pain is the first such collaboration between APS and AAPM. It is the sixth evidenced-based, pain management clinical practice guideline published by APS. Others have covered sickle-cell disease, arthritis, cancer, fibromyalgia, and low back pain.

### **Growth factor protects key brain cells in Alzheimer's models**

#### ***UC San Diego study in animals may pave way for novel approach to treating Alzheimer's disease***

Memory loss, cognitive impairment, brain cell degeneration and cell death were prevented or reversed in several animal models after treatment with a naturally occurring protein called brain-derived neurotrophic factor (BDNF). The study by a University of California, San Diego-led team – published in the February 8, 2009 issue of *Nature Medicine* – shows that BDNF treatment can potentially provide long-lasting protection by slowing, or even stopping the progression of Alzheimer's disease in animal models.

"The effects of BDNF were potent," said Mark Tuszynski, MD, PhD, professor of neurosciences at the UC San Diego School of Medicine and neurologist at the Veterans Affairs San Diego Health System. "When we administered BDNF to memory circuits in the brain, we directly stimulated their activity and prevented cell death from the underlying disease."

BDNF is normally produced throughout life in the entorhinal cortex, a portion of the brain that supports memory. Its production decreases in the presence of Alzheimer's disease. For these experiments, the researchers injected the BDNF gene or protein in a series of cell culture and animal models, including transgenic mouse models of Alzheimer's disease; aged rats; rats with induced damage to the entorhinal cortex; aged rhesus monkeys, and monkeys with entorhinal cortex damage.

In each case, when compared with control groups not treated with BDNF, the treated animals demonstrated significant improvement in the performance of a variety of learning and memory tests. Notably, the brains of the treated animals also exhibited restored BDNF gene expression, enhanced cell size, improved cell signaling, and activation of function in neurons that would otherwise have degenerated, compared to untreated animals. These benefits extended to the degenerating hippocampus where short-term memory is processed, one of the first regions of the brain to suffer damage in Alzheimer's disease.

The demonstration of the effectiveness and safety of BDNF administration in animals provides "a rationale for exploring clinical translation" to humans, the team concludes, suggesting that the protective and restorative effects of BDNF on damaged neurons and neuronal signaling may offer a new approach to treating Alzheimer's disease.

This work builds on previous studies by Tuszynski and others, demonstrating the therapeutic affects of nerve growth factor (NGF) administered to patients with Alzheimer's disease. In 2001, Tuszynski and his team at UC San Diego Medical Center performed the first surgical implants of NGF genes into the brains of Alzheimer's patients, with follow-up results showing these patients experienced a possible slowing in cognitive decline and

increased metabolic function in the brain. The NGF studies continue today, with Phase 2, multi-center studies currently underway.

"NGF therapy aims to stimulate the function of specific cholinergic neurons, which are like the air traffic controllers of the brain, helping to direct the activities of cells in broad regions of the brain," Tuszynski explained. However, he added that the benefits of NGF therapy, if validated in ongoing trials, will not be curative. Eventually, the effect of the NGF "boost" will be countered by the widespread death of neurons in the cerebral cortex as a result of advancing Alzheimer's disease.

"In contrast, BDNF acts directly on dying cells in specific memory circuits of the brain," Tuszynski said. "In this series of studies, we have shown that BDNF targets the cortical cells themselves, preventing their death, stimulating their function, and improving learning and memory. Thus, BDNF treatment can potentially provide long-lasting protection by slowing, or even stopping disease progression in the cortical regions that receive treatment."

The protective and restorative effects of BDNF occurred independently of the build-up of amyloid, a protein that accumulates in the brain to form plaques in Alzheimer's disease. Many current experimental treatments for Alzheimer's disease target amyloid production, so the potential role of BDNF as an alternative protective intervention is of great potential interest, said Tuszynski. Because BDNF targets a different set of disease mechanisms than amyloid modulation, there is also potential to combine BDNF and amyloid-based treatments, theoretically providing a two-pronged attack on the disease.

*The study was supported by the National Institutes of Health, the California Regional Primate Research Center, the Veterans Administration, the Alzheimer's Association, the State of California, the Dr. Miriam and Sheldon G. Adelson Medical Research Foundation and the Shiley Family Foundation. Tuszynski is scientific founder of Trophin Therapeutics, a company that may potentially benefit from the research results.*

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### **That gut feeling may actually reflect a reliable memory**

EVANSTON, Ill. --- You know the feeling. You make a decision you're certain is merely a "lucky guess."

A new study from Northwestern University offers precise electrophysiological evidence that such decisions may sometimes not be guesswork after all.

The research utilizes the latest brain-reading technology to point to the surprising accuracy of memories that can't be consciously accessed.

During a special recognition test, guesses turned out to be as accurate or more accurate than when study participants thought they consciously remembered.

"We may actually know more than we think we know in everyday situations, too," said Ken Paller, professor of psychology at Northwestern. "Unconscious memory may come into play, for example, in recognizing the face of a perpetrator of a crime or the correct answer on a test. Or the choice from a horde of consumer products may be driven by memories that are quite alive on an unconscious level."

The study links lucky guesses to valid memories and suggests that people need to be more receptive to multiple types of knowledge, Paller said.

Paller and Joel L. Voss, who received his Ph.D. at Northwestern and is now at the Beckman Institute, are co-investigators of the study. "An Electrophysiological Signature of Unconscious Recognition Memory" will be published online Feb. 8 by the journal *Nature Neuroscience*.

During the first part of the memory test, study participants were shown a series of colorful kaleidoscope images that flashed on a computer screen. Half of the images were viewed with full attention as participants tried to memorize them.

While viewing each of the other images, they heard a spoken number, such as 3, 8 or 4, which they had to keep in mind until the next trial, when they indicated whether it was odd or even. On every trial they had to listen to a new number and press a button to complete the number task.

In other words, they could focus on memorizing half of the images but were greatly distracted from memorizing the others.

A short time later, they viewed pairs of similar kaleidoscope images in a recognition test.

"Remarkably, people were more accurate in selecting the old image when they had been distracted than when they had paid full attention," Paller said. "They also were more accurate when they claimed to be guessing than when they registered some familiarity for the image."

Splitting attention during a memory test usually makes memory worse. "But our research showed that even when people weren't paying as much attention, their visual system was storing information quite well," Paller said.

When implicit recognition took place, EEG signals were recorded from a set of electrodes placed on each person's head. The brain waves were distinct from those associated with conscious memory experiences. A unique signal of implicit recognition was seen a quarter of a second after study participants saw each old image.

The findings include memory effects and brain-wave effects. The memory effects with kaleidoscopes were found in two groups of 24 people each (published in a prior paper: Voss & Paller, 2008). The brain-wave effects were found in one group of 12 subjects. Both memory and brain-wave effects were also seen in pilot studies not reported in either paper.

"The novel results show that when people try to remember, they can know more than they think they know," Paller said.

The study builds upon a body of research that shows that amnesia victims with severe memory problems often have strong implicit memories.

The study suggests that we shouldn't rely only on conscious memory, Paller concludes. "It suggests that we also need to develop our intuitive nature and creativity. Intuition may have an important role in finding answers to all sorts of problems in everyday life -- including big ones such as our ailing economy."

### **While focusing on heart disease, researchers discover new tactic against fatal muscular dystrophy**

#### ***Drugs similar to 1 in trials for heart disease may slow muscle loss in most common form of muscular dystrophy***

NEW YORK – Based on a striking similarity between heart disease and Duchenne muscular dystrophy, researchers at Columbia University Medical Center have discovered that a new class of experimental drugs for heart failure may also help treat the fatal muscular disorder.

At first glance, heart failure and the muscle-wasting Duchenne disease couldn't appear more dissimilar. Duchenne affects boys usually before the age of 6, destroying their muscle cells. The boys become progressively weaker through their teens and usually die in their twenties. In people without Duchenne, heart failure typically starts much later in life, robbing the heart's pumping ability in the 7th, 8th or 9th decade of life.

But the new study found that the muscle cells affected in both diseases have sprung the same microscopic leak that ultimately weakens skeletal muscle in Duchenne and cardiac muscle in heart failure. The leak lets calcium slowly seep into the skeletal muscle cells, which are damaged from the excess calcium in Duchenne. In people with chronic heart failure, a similar calcium leak continuously weakens the force produced by the heart and also turns on a protein-digesting enzyme that damages its muscle fibers.

Andrew Marks, M.D., the study's leader, hypothesized that a new class of experimental drugs developed at CUMC – which he had designed to plug the leak in the heart – could also work for Duchenne.

The drugs, when given to mice with Duchenne, dramatically improved muscle strength and reduced the number of damaged muscle cells.

"This was extremely exciting to us," says Dr. Marks, chair of the Department of Physiology & Cellular Biophysics and Clyde and Helen Wu Professor of Molecular Cardiology. "If it works in people, our drug won't be a cure, but it could slow the pace of muscle degeneration and extend the lives of people with Duchenne."

The study was published online Feb. 8 in Nature Medicine. Though the new drugs are not FDA-approved or currently available for Duchenne patients, a similar drug that was used in the Duchenne study is undergoing Phase I safety trials, and later this year trials will begin for heart failure.