

## **Fibromyalgia can no longer be called the 'invisible' syndrome**

### ***Molecular imaging uncovers evidence that symptoms are related to functional brain abnormalities, according to article in the Journal of Nuclear Medicine***

Reston, Va. - Using single photon emission computed tomography (SPECT), researchers in France were able to detect functional abnormalities in certain regions in the brains of patients diagnosed with fibromyalgia, reinforcing the idea that symptoms of the disorder are related to a dysfunction in those parts of the brain where pain is processed.

"Fibromyalgia is frequently considered an 'invisible syndrome' since musculoskeletal imaging is negative," said Eric Guedj, M.D., and lead author of the study. "Past imaging studies of patients with the syndrome, however, have shown above-normal cerebral blood flow (brain perfusion) in some areas of the brain and below-normal in other areas. After performing whole-brain scans on the participants, we used a statistical analysis to study the relationship between functional activity in even the smallest area of the brain and various parameters related to pain, disability and anxiety/depression."

In the study, which was reported in the November issue of *The Journal of Nuclear Medicine*, 20 women diagnosed with fibromyalgia and 10 healthy women as a control group responded to questionnaires to determine levels of pain, disability, anxiety and depression. SPECT was then performed, and positive and negative correlations were determined.

The researchers confirmed that patients with the syndrome exhibited brain perfusion abnormalities in comparison to the healthy subjects. Further, these abnormalities were found to be directly correlated with the severity of the disease. An increase in perfusion (hyperperfusion) was found in that region of the brain known to discriminate pain intensity, and a decrease (hypoperfusion) was found within those areas thought to be involved in emotional responses to pain.

In the past, some researchers have thought that the pain reported by fibromyalgia patients was the result of depression rather than symptoms of a disorder. "Interestingly, we found that these functional abnormalities were independent of anxiety and depression status," Guedj said.

According to Guedj, disability is frequently used in controlled clinical trials to evaluate response to treatment. Because molecular imaging techniques such as SPECT can help predict a patient's response to a specific treatment and evaluate brain-processing recovery during follow-up, it could prove useful when integrated into future pharmacological controlled trials.

"Fibromyalgia may be related to a global dysfunction of cerebral pain-processing," Guedj added. "This study demonstrates that these patients exhibit modifications of brain perfusion not found in healthy subjects and reinforces the idea that fibromyalgia is a 'real disease/disorder.'"

According to the National Institute of Arthritis and Musculoskeletal and Skin Diseases, fibromyalgia syndrome is a common and chronic disorder characterized by widespread muscle pain, fatigue and multiple tender points. Tender points are specific places - for example, on the neck, shoulders, back, hips, and upper and lower extremities - where people with fibromyalgia feel pain in response to slight pressure. The syndrome is one of the most common causes of musculoskeletal pain and disability and affects three to six million, or as many as one in 50, Americans. Between 80 and 90 percent of those diagnosed are women.

Although fibromyalgia is often considered an arthritis-related condition, it does not cause inflammation or damage to the joints, muscles or other tissues. Like arthritis, however, the significant pain and fatigue caused by fibromyalgia can interfere with a person's ability to carry out daily activities.

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## **Snakebite is a neglected threat to global public health**

Snakebites cause considerable death and injury worldwide and pose an important yet neglected threat to public health, says new research published in this week's *PLoS Medicine*. The study used the most comprehensive methods yet to estimate that at least 421,000 envenomings and 20,000 deaths from snakebites occur each year, especially in South and South East Asia and sub-Saharan Africa.

To estimate death and injury from snakebite, Janaka de Silva (University of Kelaniya, Sri Lanka) and colleagues conducted a systematic review of the scientific literature, reviewed county-specific mortality data from databases maintained by United Nations organizations, and identified unpublished information from Ministries of Health, National Poison Centres, and snakebite experts on snakebites in countries that do not have reliable data on snakebite incidence and mortality.

This data retrieval produced information for many of the world's 227 countries, which were grouped into 21 geographical regions. The researchers estimate that 421,000 envenomings and 20,000 deaths occur worldwide from snakebite each year, but warn that these figures may be as high as 1,841,000 envenomings and 94,000 deaths, especially in areas of sub-Saharan Africa and South Asia where antivenoms are hard to obtain. India has the highest estimated annual envenomings and deaths: 81,000, and 11,000 respectively.

In a related Perspective article, Jean-Philippe Chippaux from the Institut de Recherche pour le Développement in La Paz, Bolivia and uninvolved in the research, argues that this study is a "preliminary but essential step in improving accessibility of antivenoms and the treatment of snakebite." Dr. Chippaux notes the dire situation of antivenom availability and cost in Africa - a situation that could be worsened by the current global economic crisis - where the price of a vial of antivenom is the equivalent of several months of income for most rural families. Better information on the global burden of snakebite would help understand how much antivenom needs to be produced and in what areas it needs to be distributed, he says. As de Silva and colleagues conclude, despite their careful methodology, more population-based studies of incidence and mortality from snakebite are urgently needed.

- Figure 5 from the paper: <http://www.plos.org/press/plme-05-11-de-silva-fig-5.jpg>

**Legend: Regional Estimates of Envenomings Due to Snakebite**

- Figure 7 from the paper: <http://www.plos.org/press/plme-05-11-de-silva-fig-7.jpg>

**Legend: Regional Estimates of Deaths Due to Snakebite**

*Citation: Kasturiratne A, Wickremasinghe AR, de Silva N, Gunawardena NK, Pathmeswaran A, et al. (2008) Estimation of the global burden of snakebite. PLoS Med 5(11): e218. doi:10.1371/journal.pmed.0050218*

<http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0050218>

## **MIT pieces together the mechanism that allows 2 pacemakers to control breathing**

CAMBRIDGE, Mass. -- Two pacemakers in the brain work together in harmony to ensure that breathing occurs in a regular rhythm, according to new research from MIT scientists.

That cooperation provides critical backup during respiratory stress, from the early trauma of birth to intense exercise and oxygen shortages, said Chi-Sang Poon, principal research scientist at the Harvard-MIT Division of Health Sciences and Technology (HST).

"The two-pacemaker system provides robustness and redundancy that protects us against a number of challenges from childhood to adulthood," said Poon, senior author of a paper on the work appearing in the online edition of the Proceedings of the National Academy of Sciences the week of Nov. 3.

Abnormalities of the two pacemakers may be related to some cases of "crib death" in babies and some forms of central sleep apnea, which can affect premature infants and the elderly, Poon said.

Scientists have known that two areas of the brain, the pre-Botzinger complex (preBotC) and the parafacial respiratory group (pFRG), control breathing. However, researchers have hotly debated how these two regions work together, and which one plays a greater role in setting the pace.

The new MIT model, which Poon has dubbed the "handshake model," reconciles several different views.

In Poon's model, developed with graduate student Steffen Wittmeier, lead author of the paper, both brain regions work together to regulate respiration during infancy, but the preBotC takes control during adulthood.

Early in life, both pacemakers are needed. After birth, and throughout infancy, the pFRG triggers preBotC, resulting in strong, rhythmic breaths. Without pFRG, breathing can be weak and erratic, Poon said.

However, after childhood, the preBotC region takes over as the dominant pacemaker. Only under respiratory stress, such as during shortage of oxygen, does pFRG kick in and help regulate breathing rhythm.

The new model is called the "handshake model" because the two pacemakers send signals back and forth to trigger each other. "It's not just a one-way street," Poon said.

The fail-safe network provides critical backup and appears to be evolutionarily conserved, as it is also found in reptiles, birds and amphibians.

During infancy, when both pacemakers are regulating breathing, the pFRG takes the lead role, exciting the preBotC to initiate inhalation. During inhalation, the preBotC inhibits pFRG but the pFRG rebounds at the end of inhalation. The process starts over when pFRG excites preBotC again at the end of exhalation.

Later on, in adulthood, pFRG becomes less important and preBotC becomes more independent. The exception is during respiratory stress, such as a shortage of oxygen. In those situations, the system becomes a "reverse handshake," with both pacemakers functioning and preBotC taking the lead.

"This is a beautiful example of a yin-yang relationship," said Poon, with pacemakers exciting and inhibiting one another. "You want to be stable so you can have harmony."

*Other authors of the paper are Gang Song, research scientist in HST, and James Duffin of the University of Toronto. The research was funded by the National Institutes of Health.*

## **Women have more diverse hand bacteria than men, says CU-Boulder study**

### ***Study also shows participants shared an average of only 13 percent of bacteria species with each other***

A new University of Colorado at Boulder study indicates that not only do human hands harbor far higher numbers of bacteria species than previously believed, women have a significantly greater diversity of microbes on their palms than men.

The results have implications for better understanding human bacteria and should help establish a "healthy baseline" to detect microbial community differences on individuals that are associated with a wide variety of human diseases, said CU-Boulder Assistant Professor Noah Fierer, lead study author. A paper on the subject by the CU-Boulder researchers was published online Nov. 3 in the Proceedings of the National Academy of Sciences.

Using powerful gene sequencing techniques, the team found a typical hand in the new study had roughly 150 different species of bacteria living on it, said Fierer of CU-Boulder's ecology and evolutionary biology department. While the researchers detected and identified more than 4,700 different bacteria species across 102 human hands in the study, only five species were shared among all 51 participants.

"The sheer number of bacteria species detected on the hands of the study participants was a big surprise, and so was the greater diversity of bacteria we found on the hands of women," said Fierer. The study also showed that the diversity of bacteria on individual hands was not significantly affected by regular hand washing, he said.

The 332,000 gene sequences obtained by the CU team were nearly 100 times greater than those obtained from other studies of skin bacteria also obtained by sampling the entire DNA of microbe communities, known as "metagenomics." The new CU-Boulder study also confirms that standard skin culturing of human skin bacteria, a technique used by many labs, dramatically underestimates the full extent of microbial diversity, Fierer said.

Co-authors on the PNAS study included Micah Hamady of CU-Boulder's computer science department, Christian Lauber of CU-Boulder's Cooperative Institute for Research in Environmental Sciences and CU-Boulder chemistry and biochemistry Assistant Professor Rob Knight. The study was funded primarily by the National Institutes of Health and the National Science Foundation.

Fierer speculated that skin pH may play a role in the higher bacterial diversity on women's hands, since men generally have more acidic skin, and other research has shown microbes are less diverse in more acidic environments. The findings also could be due to differences in sweat and oil gland production between men and women, the frequency of moisturizer or cosmetics applications, skin thickness or hormone production, he said.

The right and left palms of the same individual shared an average of only 17 percent of the same bacteria types, said Knight. Study volunteers, all CU undergraduates, shared an average of only 13 percent of bacteria species with each other, he said.

Although the composition of bacterial communities on dominant and non-dominant hands of subjects was significantly different, diversity levels were similar, Fierer said. The differences found between dominant and non-dominant hands were likely due to environmental conditions like oil production, salinity, moisture or variable environmental surfaces touched by either hand of an individual, he said.

While some groups of bacteria were less abundant following hand washing, others were more abundant, said Knight, who stressed that regular hand washing with anti-bacterial soap is beneficial. "The vast majority of bacteria are non-pathogenic, and some bacteria even protect against the spread of pathogens," Knight said. "From a public health standpoint, regular hand washing has a very positive effect."

"Although hand washing altered community composition, overall levels of bacterial diversity were unrelated to the time since the last hand washing," wrote the researchers in PNAS. "Either the bacterial colonies rapidly re-establish after hand washing, or washing (as practiced by the students included in this study) does not remove the majority of bacteria taxa found on the skin surface."

The CU-Boulder team used the metagenomic survey to simultaneously analyze all of the bacteria on a given palm surface, said Knight. In simple terms, the effort involved isolating and amplifying tiny bits of microbial DNA, then building complementary DNA strands with a high-powered sequencing machine that allowed the team to identify different families, genera and species of bacteria from the sample.

Knight recently received a \$1.1 million NIH grant to develop new computational tools to better understand the composition and dynamics of microbial communities. He has been developing novel methods to tag DNA samples with error-correcting "barcodes" to obtain more accurate sequencing data.

The richness of bacteria types on the palm was three times higher than that found on the forearm and elbow, according to the researchers. The total diversity of hand bacteria appears to match or exceed levels of bacteria colonizing other parts of the body, including the esophagus, the mouth and lower intestine, Fierer said.

"I view humans as 'continents' of microscopic ecological zones with the kind of diversity comparable to deep oceans or tropical jungles," Fierer said. "Today we have the ability to answer large-scale questions about these complex microbial communities and their implications for human health that we weren't even asking six months or a year ago."

### **Grandparents a safe source of childcare**

#### ***Contrary to popular belief, grandparent care is not associated with more childhood injuries***

For working parents, having grandparents as caregivers can cut the risk of childhood injury roughly in half, according to a new study by researchers from the Johns Hopkins Bloomberg School of Public Health. Compared to organized daycare or care by the mother or other relatives, having a grandmother watch a child was associated with a decreased risk of injury for the child. The study is among the first to examine the relationship between grandparents' care and childhood injury rates. The results are published in the November 2008 issue of *Pediatrics*.

In addition to source of caregiving, researchers examined the connections between family structure and the likelihood of injury. According to the researchers, the odds of injury were significantly greater among children whose parents never married compared with children whose mothers stayed married throughout the child's life. Similarly, odds of injury were greater for children living in homes in which the father did not co-reside. These associations were independent of family income.

"Recent growth in the number of grandparents providing childcare has some observers concerned they don't adhere to modern safety practices," said lead study author David Bishai, MD, PhD, MPH, a professor with the Bloomberg School's Department of Population, Family and Reproductive Health. "To the contrary, this research tells us not only is there no evidence to support this assumption, but families that choose grandparents to care for their children experience fewer child injuries."

Bishai and colleagues analyzed data from the National Evaluation of the Healthy Steps for Young Children Program, which includes information on over 5,500 newborns enrolled in 15 U.S. cities in 1996-97 with follow-up for 30-33 months. Data on child care arrangements reported by the mother were linked to claims reporting children's office visits, allowing researchers to identify medically attended injuries.

"As injuries are the number one cause of death for children in the United States, it's critical we continue to determine risk and protective factors," said study co-author Andrea C. Gielen, ScD, ScM, a co-author of the study and director of the Center for Injury Research and Policy in the Department of Health Policy and Management at the Bloomberg School of Public Health. "Additional studies of how households choose relatives to watch their children and the actual caregiving style of grandparents are warranted because the protective effect of grandparents may depend on choosing the right grandparent."

*Additional authors of "Risk Factors for Unintentional Injuries in Children: Are Grandparents Protective" are Jamie L. Trevitt, MPP, Yiduo Zhang, PhD, Lara B. McKenzie, PhD, Tama Leventhal, PhD, and Bernard Guyer, MD, MPH. The research was funded by a grant from the Maternal and Child Health Bureau R40MC05475.*

### **How HIV vaccine might have increased odds of infection**

In September 2007, a phase II HIV-1 vaccine trial was abruptly halted when researchers found that the vaccine may have promoted, rather than prevented, HIV infection. A new study by a team of researchers at the Montpellier Institute of Molecular Genetics in France shows how the vaccine could have enhanced HIV infection. The study, lead by Matthieu Perreau, will be published online on November 3 of the *Journal of Experimental Medicine*.

The HIV-1 vaccine used in Merck's STEP trial relied on a weakened form of a common cold virus, Adenovirus 5 (Ad5), to carry bits of HIV into the body. Those bits would presumably trigger the immune system to fight off later infection with the virus. One worry about the Ad5 vaccine vector was that widespread immunity to adenoviruses might cause the vaccine to be ousted from the body before an anti-HIV response could develop. Yet three years after the trial began, researchers realized that more of the vaccine recipients who had prior immunity to adenoviruses had been infected with HIV than those without such immunity.

The new study shows how the presence of long-lasting Ad5-specific antibodies - generated during natural infections with adenoviruses - may have altered the immune response to the HIV vaccine. In the presence of antibodies from Ad5-immune individuals, HIV infection spread through cell cultures three times faster than without them. The antibodies tethered the Ad5-HIV vaccine to receptors on the surface of specialized immune cells, called antigen-presenting cells (APCs), thus facilitating entry of the vaccine into the cell. Once inside, components of the vaccine then activated these cells, allowing the APCs in turn to activate T cells. Since HIV prefers to infect active T cells, the virus was thus provided with more cells to infect.

Merck's vaccine may have made it to phase II trials because primates, used in the phase 1 trials, don't naturally come in contact with human adenoviruses, and therefore the potential problem went unrecognized.

## **Minor shift in vaccine schedule has potential to reduce infant illness, death**

WINSTON-SALEM, N.C. – A new study by researchers at Wake Forest University School of Medicine and Vanderbilt University suggests that protecting infants from a common, highly contagious and even deadly disease may be as easy as administering a routine vaccine two weeks earlier than it is typically given.

The shift has the potential to prevent at least 1,236 cases of pertussis, 898 hospitalizations and seven deaths attributable to pertussis each year in the United States, said Timothy R. Peters, M.D., co-lead author and an assistant professor of pediatrics at Brenner Children's Hospital, which is part of Wake Forest Baptist.

"Rates of pertussis, which can be life-threatening in young infants, are increasing," Peters said. "Pertussis vaccine has been highly effective in defending children against this disease, and we find that modest adjustments in the timing of vaccine administration may offer enhanced protection to very young infants who are especially susceptible to severe disease."

The study appears in the November issue of *Pediatrics*.

Pertussis, commonly known as "whooping cough" or "the 100-day cough," is a disease marked by severe coughing. Young infants are at the highest risk for pertussis-related complications, including pneumonia, seizures, brain swelling and even death. Among infants in the United States, the incidence of pertussis peaks at 1 month of age and progressively decreases over the next year. Pneumonia is the most common complication and cause of infant pertussis-related deaths and, in 2003 13 children died from pertussis. Most deaths occur among unvaccinated children or infants too young to be vaccinated.

While there is no lifelong protection against whooping cough, immunization is the best preventative measure. Current recommendations suggest five doses of the diphtheria-tetanus-acellular pertussis (DTaP) vaccine at 2, 4 and 6 months of age, with booster doses at 15 to 18 months and 4 to 6 years. Current recommendations also allow for administration of the first dose as early as 6 weeks of age, with the second and third doses at 3.5 months and 5.5 months.

The 2004 National Immunization Survey estimated that only 88 percent of infants had received one dose of DTaP vaccine by 3 months of age, 76 percent of infants had received two doses of DTaP vaccine by 5 months of age, and a mere 66 percent of infants had received the first three vital doses of DTaP vaccine by 7 months of age.

In this study, researchers sought to estimate the potential benefit of accelerating first dose administration from 2 months to 6 weeks of age.

"While two weeks may seem negligible, this change would reduce the time that a 2-month-old infant is completely without pertussis vaccine protection by 25 percent," Peters said. "Because pertussis so greatly threatens very young infants, the benefit of earlier vaccination may result in a significant decrease in severe pertussis disease nationally, and may be an especially useful approach during outbreaks of pertussis."

Researchers reviewed existing data to estimate current rates of pertussis infections, hospitalizations and deaths according to age and infant population in the United States in 2004. The data led researchers to expect that acceleration of the second and third doses by two weeks would prevent an additional 923 cases, 520 hospitalizations, and two deaths, according to the study.

Although administration of the first dose of the pertussis vaccine at 6 weeks of age is a change from the current routine practice of administration at 2 months, the minor dose acceleration falls within the current recommendations of the Advisory Committee on Immunization Practices and the American Academy of Pediatrics for the childhood vaccination schedule, and should have little impact on medical providers or on the number of outpatient physician visits for vaccines. All of the vaccines that are routinely given at a 2-month "well child" visit could be given at a replacement 6-week visit and still be in compliance with accepted vaccine schedule recommendations, the researchers report.

The researchers advise that the study's results are based on nationally reported data and additional studies would be necessary to evaluate the actual effects of this intervention. In estimating the impact of accelerating the vaccine schedule, they used conservative criteria to reduce the chance of overestimation but admit they may have underestimated the true benefit in the process.

"Vaccines have tremendous potential to reduce disease rates and, as new data become available, practices should continue to modify their vaccination practices to optimize the impact," the researchers write in their findings. "Changes in vaccination schedules involve virtually no cost and have the potential for great benefit. This relatively minor change in pediatric practice could reduce the burdens on families and society of pertussis and perhaps of other vaccine-preventable diseases."

*Co-researchers included Katherine A. Poehling, M.D., M.P.H., of Wake Forest University School of Medicine; and Myrick C. Shinall, Jr., B.A., Yuwei Zhu, M.D., M.S., and Qingxia Chen, Ph.D., all of Vanderbilt University.*

## Rainforest fungus makes diesel

A unique fungus that makes diesel compounds has been discovered living in trees in the rainforest, according to a paper published in the November issue of Microbiology. The fungus is potentially a totally new source of green energy and scientists are now working to develop its fuel producing potential.

"This is the only organism that has ever been shown to produce such an important combination of fuel substances," said Professor Gary Strobel from Montana State University. "The fungus can even make these diesel compounds from cellulose, which would make it a better source of biofuel than anything we use at the moment."

The fungus, which has been named *Gliocladium roseum*, produces a number of different molecules made of hydrogen and carbon that are found in diesel. Because of this, the fuel it produces is called "myco-diesel".

"*Gliocladium roseum* lives inside the Ulmo tree in the Patagonian rainforest. We were trying to discover totally novel fungi in this tree by exposing its tissues to the volatile antibiotics of the fungus *Muscodor albus*. Quite unexpectedly, *G. roseum* grew in the presence of these gases when almost all other fungi were killed. It was also making volatile antibiotics. Then when we examined the gas composition of *G. roseum*, we were totally surprised to learn that it was making a plethora of hydrocarbons and hydrocarbon derivatives. The results were totally unexpected and very exciting and almost every hair on my arms stood on end!"

Many microbes produce hydrocarbons. Fungi that live in wood seem to make a range of potentially explosive compounds. In the rainforest, *G. roseum* produces lots of long chain hydrocarbons and other biological molecules. When the researchers grew it in the lab, it produced fuel that is even more similar to the diesel we put in our cars.

"When crops are used to make biofuel they have to be processed before they can be turned into useful compounds by microbes," said Professor Strobel. "*G. roseum* can make myco-diesel directly from cellulose, the main compound found in plants and paper. This means if the fungus was used to make fuel, a step in the production process could be skipped."

Cellulose, lignin and hemicellulose make up the cell walls in plants. Lignin is the glue that holds the cellulose fibres together and makes the plant stand up. These compounds form the part of the plant that most animals cannot digest. They makes up non-foodstuffs like stalks, sawdust and woodchip. Nearly 430 million tonnes of plant waste are produced from just farmland every year; a huge amount to recycle. In current biofuel production, this waste is treated with enzymes called cellulases that turn the cellulose into sugar. Microbes then ferment this sugar into ethanol that can be used as a fuel.

"We were very excited to discover that *G. roseum* can digest cellulose. Although the fungus makes less myco-diesel when it feeds on cellulose compared to sugars, new developments in fermentation technology and genetic manipulation could help improve the yield," said Professor Strobel. "In fact, the genes of the fungus are just as useful as the fungus itself in the development of new biofuels."

"The discovery also questions our knowledge of the way fossil fuels are made. The accepted theory is that crude oil, which is used to make diesel, is formed from the remains of dead plants and animals that have been exposed to heat and pressure for millions of years," said Professor Strobel. "If fungi like this are producing myco-diesel all over the rainforest, they may have contributed to the formation of fossil fuels."

## Consuming small amounts of caffeine when pregnant may affect the growth of an unborn child

### ***Research paper: Human maternal caffeine intake during pregnancy and the risk of fetal growth restriction: Large prospective study***

Consuming caffeine at any time during pregnancy is associated with an increased risk of fetal growth restriction (low birth weight), according to research published on [bmj.com](http://bmj.com) today.

Although some previous studies have also shown this, this BMJ study additionally shows that any amount and type of caffeine intake - from tea, cola, chocolate, cocoa, and some prescription drugs, as well as coffee - is linked with relatively slower fetal growth.

Dr Justin Konje and colleagues from the University of Leicester as well as collaborators from the University of Leeds, examined the association of maternal caffeine intake and individual caffeine metabolism on birth weight.

From two large teaching hospitals in the UK between September 2003 and June 2006 the authors recruited 2645 low risk pregnant women of average age 30, who were between 8-12 weeks pregnant. They used a caffeine assessment tool (CAT) to record caffeine intake from all possible dietary sources in the four weeks before and throughout pregnancy, and also used a saliva sample test to calculate individual caffeine metabolism.

The researchers report that the average caffeine intake during pregnancy was 159mg/day, much lower than the limit of 300mg/day recommended by the UK government's Food Standards Agency. Interestingly, 62% of

the caffeine use reported came from tea. Other sources were coffee (14%), cola (12%), chocolate (8%), and soft drinks (2%).

Most of the babies were born at full term, with an average birth weight of 3450g (which is around the UK average), while 4% were born prematurely, 0.3% were stillborn, and 0.7% were miscarried late. Overall, the results confirmed that these were low risk pregnancies. However, the authors found a 'dose-response relationship', showing that increasing caffeine intake was associated with increasing risk of fetal growth restriction (FGR).

Compared to pregnant women consuming less than 100mg/day (the equivalent of less than one cup of coffee), the risk estimates of having a lower birth weight baby increased by 20% for intakes of 100-199mg/day, by 50% for those taking between 200-299mg/day, and by 40% for over 300mg/day.

There was no level of caffeine intake at which the increased risk of FGR stopped increasing during pregnancy. Caffeine consumption of more than 100mg/day, the equivalent of one cup of coffee, was associated with a reduction in birth weight of 34-59g in the first, 24-74g in the second, and about 66-89g in the third trimesters. This effect was significant and consistent across all trimesters with consumption of over 200mg/day. The authors also noted that the link between caffeine and FGR was stronger in women who metabolised caffeine more quickly.

The authors explain that, although these reductions in birth weight may seem small given that the average birth weight is over 3kg, a drop of 60-70 g might be important for a baby that was already small and at risk. Pregnant women should make every effort to significantly reduce their caffeine consumption before and during pregnancy, they warn. In light of this evidence, the UK Government's Food Standards Agency are altering their guidance on the recommended daily limit of caffeine consumption and reducing it from 300mg to 200mg.

These findings will reinforce the concern that caffeine is a potential fetotoxic substance, say Professor Jørn Olsen and Professor Bodil Hammer Bech, in an accompanying editorial. But the advice offered by the authors could unnecessarily frighten women who have consumed some caffeine during pregnancy.

Pregnant women should reduce their intake of caffeine, but must not replace it with unhealthy alternatives such as alcoholic drinks or soft drinks full of sugar, they add.

### **Anti-VEGF drugs for retinal diseases could have serious side effects, scientists caution**

Boston, MA - Scientists at Schepens Eye Research Institute have found that reducing the levels of vascular endothelial growth factor (VEGF), which is best known as a stimulator of new blood vessel growth, in adult mice causes the death of photoreceptors and Muller glia - cells of the retina that are essential to visual function. This finding, published in the November 3, 2008 PLoS ONE, holds implications for the chronic use of promising new anti-VEGF drugs such as Lucentis, which eliminate abnormal and damaging blood vessel growth and leakage in the retina by neutralizing VEGF.

"The take home message of this study is that physicians should be vigilant in monitoring patients undergoing anti-VEGF treatments for any possible signs of these side effects," says Principal Investigator Patricia D'Amore, Senior Scientist at Schepens Eye Research Institute. "Drugs such as Lucentis are very good at reducing the edema (fluids) and eliminating the abnormal blood vessels that characterize wet macular degeneration, but our results suggest that there could be unanticipated side effects."

Scientists have long known that VEGF is essential for normal development of the vascular system and for wound healing. It triggers the formation of new blood vessels that nourish the growing body and heal organs and tissues. VEGF also stimulates--in an apparent misguided attempt to heal perceived damage in the retina--the growth of abnormal blood vessels that leak and damage delicate retinal tissue.

However, a growing body of evidence also indicates that beyond its impact on blood vessel growth, VEGF may play other vital roles in the adult body and eye, so that eliminating the growth factor might lead to unexpected consequences.

Given the popularity and promise of the new anti-VEGF drugs for the treatment of macular degeneration, D'Amore and her team believed that investigating the broader role of this growth factor in the normal adult retina was critical. She and her laboratory mimicked the action of the anti-VEGF drugs by introducing into adult mice a soluble VEGF receptor, known as sFlt1, which binds and neutralizes the VEGF-- in much the same way that Lucentis does in the eye.

After two weeks, the team found no effect on blood vessels of the inner retina, but did find a significant increase in the number of dying cells of the inner and outer nuclear layers which include amacrine cells that participate in transmitting the visual signal; Muller cells that also participate in the visual signal and support the photoreceptors; and, photoreceptors, which are responsible for color and night vision. The team then used electroretinograms to measure visual function and found a significant loss in visual function. Consistent with

these observations, they discovered that both photoreceptors and Muller cells express VEGFR2, the major VEGF signaling receptor and they found that neighboring Muller cells express VEGF.

Parallel studies in tissue culture demonstrated that suppressing VEGF in Muller cells led to Muller cell death, indicating an autocrine role for VEGF in Muller cells (i.e. Muller cells both make VEGF and use it for survival). Further, they used cultures of freshly isolated photoreceptors to show that VEGF can act as a protectant for these cells.

"Insight into the complex role of VEGF in the eye and in other parts of the body indicates that increased care should be taken in the long-term use of these drugs and that this new information should be considered in the design of future clinical studies to ensure that these possible side effects are taken into account," says D'Amore.

"Mice eyes differ from human eyes in many ways, so we cannot directly extrapolate these results to humans, but this study is an important heads-up that clinical application of anti-VEGF therapy in the eye needs to proceed with caution," she adds.

From a clinical perspective, Dr. Delia Sang of Ophthalmic Consultants of Boston points out that the use of anti-VEGF therapy in the treatment of patients with wet macular degeneration has revolutionized outcomes in this disease. However, in light of the work of Dr. D'Amore and others, in elucidating possible systemic and ocular side effects of these drugs, "caution must be exercised in identifying patients at increased risk of problems with long-term VEGF blockade, and potential side effects must be detected early in the assessment of patients who will require repeated dosages of anti-VEGF agents."

The study is also relevant to the drug Avastin, which was initially approved for intravenous use as an anti-angiogenic agent in the treatment of cancer, but is also widely used intravitreally for the treatment of wet AMD because of its similar mode of action and much lower cost.

*The next steps in D'Amore's research will include investigating the specific functions of VEGF in the eye.*

*Authors of the study include: Magali Saint-Geniez (1,2), Arindel S. R. Maharaj (1), Tony E. Walshe (1,2), Budd A. Tucker (1,2), Eiichi Sekiyama (1,2), Tomoki Kurihara (1), Diane C. Darland (4), Michael J. Young (1,2), Patricia A. D'Amore (1,2,3)*

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### **Surgical Removal of Small Colon Polyps is Costly and Unnecessary**

Polypectomy (the surgical removal of polyps by colonoscopy) of small polyps found during CT colonography is costly and unnecessary according to a study performed at the University of Wisconsin School of Medicine and Public Health in Madison, WI.

A decision analysis model was constructed to represent the clinical and economic consequences of performing three year colorectal cancer surveillance, immediate colonoscopy with polypectomy, or neither on patients who have 6-9 mm polyps found on CT colonography (CTC). The analysis model was accompanied by a hypothetical population of 100,000 60-year-old adults with 6- to 9-mm polyps detected at CTC screening. Results showed that, "by excluding large polyps and masses, CTC screening can place a patient in a very low risk category making colonoscopy for small polyps probably not warranted," said Perry J. Pickhardt, MD, lead author of the study. "Approximately 10,000 colonoscopy referrals would be needed for each theoretical cancer death prevented at a cost of nearly \$400,000 per life-year gained. We would also expect an additional 10 perforations and probably one death related to these extra colonoscopies. There may be no net gain in terms of lives - just extra costs," said Dr. Pickhardt.

"The clinical management of small polyps detected at colorectal cancer screening has provoked controversy between radiologists and gastroenterologists. Patients should be allowed to have the choice between immediate colonoscopy and imaging surveillance for one or two isolated small polyps detected at colorectal cancer screening," said Dr. Pickhardt.

CT colonography is now a recommended test for colorectal cancer screening by the American Cancer Society. "If patients with small polyps are monitored, only five percent of adults undergoing CTC screening will need to undergo immediate invasive colonoscopy," said Dr. Pickhardt.

*This study appears in the November issue of the American Journal of Roentgenology. For a copy of the full study, please contact Heather Curry via email at hcurry@arrs.org.*

### **Clinical Management of Small (6- to 9-mm) Polyps Detected at Screening CT Colonography: A Cost-Effectiveness Analysis**

*Perry J. Pickhardt<sup>1,2</sup>, Cesare Hassan<sup>3</sup>, Andrea Laghi<sup>4</sup>, Angelo Zullo<sup>3</sup>, David H. Kim<sup>1</sup>, Franco Iafrate<sup>4</sup> and Sergio Morini<sup>3</sup>  
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**OBJECTIVE.** The primary aim of this model analysis was to compare the clinical and economic impacts of immediate polypectomy versus 3-year CT colonography (CTC) surveillance for small (6- to 9-mm) polyps detected at CTC screening.

**MATERIALS AND METHODS.** A decision analysis model was constructed incorporating the expected advanced neoplasia prevalence, frequency of measurable growth, colorectal cancer (CRC) prevalence and risk, CTC performance, and costs related to CRC screening and treatment. CRC risk was assumed to be independent of advanced adenoma size, which intentionally overestimates the risk related to small polyps. Clinical effectiveness and costs for 3-year CTC surveillance versus immediate colonoscopic polypectomy were compared for a concentrated cohort of patients with 6- to 9-mm polyps. For the CTC surveillance strategy, only cases with measurable growth ( $\geq 1$  mm) at follow-up CTC were referred for polypectomy.

**RESULTS.** Without any intervention, the estimated 5-year CRC death rate from 6- to 9-mm polyps in this concentrated cohort was 0.08%, which is a sevenfold decrease over the 0.56% CRC risk for the general unselected screening population. The death rate was further reduced to 0.03% with the CTC surveillance strategy and to 0.02% with immediate colonoscopy referral. However, for each additional cancer-related death prevented with immediate polypectomy versus CTC follow-up, 9,977 colonoscopy referrals would be needed, resulting in 10 additional perforations and an incremental cost-effectiveness ratio of \$372,853.

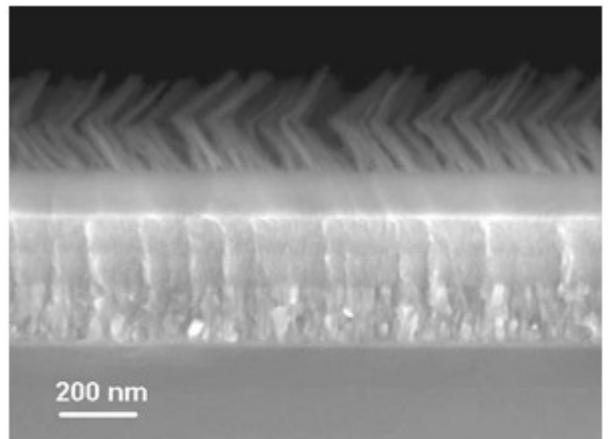
**CONCLUSION.** For patients with small (6- to 9-mm) polyps detected at CTC screening, the exclusion of large polyps ( $\geq 10$  mm) already confers a very low risk of CRC. The high costs, additional complications, and relatively low incremental yield associated with immediate polypectomy of 6- to 9-mm polyps support the practice of 3-year CTC surveillance, which allows for selective noninvasive identification of small polyps at risk.

*Keywords: colorectal cancer • cost-effectiveness • CT colonography • polyps • screening • virtual colonoscopy*

## **Solar Power Game-Changer: "Near Perfect" Absorption of Sunlight, From All Angles**

Researchers at Rensselaer Polytechnic Institute have discovered and demonstrated a new method for overcoming two major hurdles facing solar energy. By developing a new antireflective coating that boosts the amount of sunlight captured by solar panels and allows those panels to absorb the entire solar spectrum from nearly any angle, the research team has moved academia and industry closer to realizing high-efficiency, cost-effective solar power.

"To get maximum efficiency when converting solar power into electricity, you want a solar panel that can absorb nearly every single photon of light, regardless of the sun's position in the sky," said Shawn-Yu Lin, professor of physics at Rensselaer and a member of the university's Future Chips Constellation, who led the research project. "Our new antireflective coating makes this possible."



*A new antireflective coating developed by researchers at Rensselaer could help to overcome two major hurdles blocking the progress and wider use of solar power. The nanoengineered coating, pictured here, boosts the amount of sunlight captured by solar panels and allows those panels to absorb the entire spectrum of sunlight from any angle, regardless of the sun's position in the sky. Credit: Rensselaer/Shawn Lin*

Results of the year-long project are explained in the paper "Realization of a Near Perfect Antireflection Coating for Silicon Solar Energy," published this week by the journal *Optics Letters*.

An untreated silicon solar cell only absorbs 67.4 percent of sunlight shone upon it - meaning that nearly one-third of that sunlight is reflected away and thus unharvestable. From an economic and efficiency perspective, this unharvested light is wasted potential and a major barrier hampering the proliferation and widespread adoption of solar power.

After a silicon surface was treated with Lin's new nanoengineered reflective coating, however, the material absorbed 96.21 percent of sunlight shone upon it - meaning that only 3.79 percent of the sunlight was reflected and unharvested. This huge gain in absorption was consistent across the entire spectrum of sunlight, from UV to visible light and infrared, and moves solar power a significant step forward toward economic viability.

Lin's new coating also successfully tackles the tricky challenge of angles.

Most surfaces and coatings are designed to absorb light - i.e., be antireflective - and transmit light - i.e., allow the light to pass through it - from a specific range of angles. Eyeglass lenses, for example, will absorb and transmit quite a bit of light from a light source directly in front of them, but those same lenses would absorb and transmit considerably less light if the light source were off to the side or on the wearer's periphery.

This same is true of conventional solar panels, which is why some industrial solar arrays are mechanized to slowly move throughout the day so their panels are perfectly aligned with the sun's position in the sky. Without this automated movement, the panels would not be optimally positioned and would therefore absorb less

sunlight. The tradeoff for this increased efficiency, however, is the energy needed to power the automation system, the cost of upkeeping this system, and the possibility of errors or misalignment.

Lin's discovery could antique these automated solar arrays, as his antireflective coating absorbs sunlight evenly and equally from all angles. This means that a stationary solar panel treated with the coating would absorb 96.21 percent of sunlight no matter the position of the sun in the sky. So along with significantly better absorption of sunlight, Lin's discovery could also enable a new generation of stationary, more cost-efficient solar arrays.

"At the beginning of the project, we asked 'would it be possible to create a single antireflective structure that can work from all angles?' Then we attacked the problem from a fundamental perspective, tested and fine-tuned our theory, and created a working device," Lin said. Rensselaer physics graduate student Mei-Ling Kuo played a key role in the investigations.

Typical antireflective coatings are engineered to transmit light of one particular wavelength. Lin's new coating stacks seven of these layers, one on top of the other, in such a way that each layer enhances the antireflective properties of the layer below it. These additional layers also help to "bend" the flow of sunlight to an angle that augments the coating's antireflective properties. This means that each layer not only transmits sunlight, it also helps to capture any light that may have otherwise been reflected off of the layers below it.

The seven layers, each with a height of 50 nanometers to 100 nanometers, are made up of silicon dioxide and titanium dioxide nanorods positioned at an oblique angle - each layer looks and functions similar to a dense forest where sunlight is "captured" between the trees. The nanorods were attached to a silicon substrate via chemical vapor disposition, and Lin said the new coating can be affixed to nearly any photovoltaic materials for use in solar cells, including III-V multi-junction and cadmium telluride.

*Along with Lin and Kuo, co-authors of the paper include E. Fred Schubert, Wellfleet Senior Constellation Professor of Future Chips at Rensselaer; Research Assistant Professor Jong Kyu Kim; physics graduate student David Poxson; and electrical engineering graduate student Frank Mont.*

*Funding for the project was provided by the U.S. Department of Energy's Office of Basic Energy Sciences, as well as the U.S. Air Force Office of Scientific Research*

### **GSU study first to confirm long-term benefits of morphine treatment in infants**

ATLANTA – A recent study conducted by researchers at Georgia State University is the first of its kind to demonstrate that administration of preemptive morphine prior to a painful procedure in infancy blocks the long-term negative consequences of pain in adult rodents. These studies have serious implications for the way anesthetics and analgesics are administered to neonates prior to surgery. Infant rodents that did not receive preemptive pain medication prior to surgery were less sensitive to the effects of morphine in adulthood. This means that infants undergoing invasive procedures at birth that do not receive any pain medicine will require more morphine in adulthood to modulate their pain.

This study -- conducted by Anne Z. Murphy, Ph.D., a GSU Professor of Neuroscience and member of the Center for Behavioral Neuroscience, and graduate student Jamie LaPrairie -- has serious clinical implications for the more than 400,000 human infants that are admitted to a newborn intensive care unit (NICU) in the United States each year.

Past studies have shown human infants born between 25-42 weeks gestation experience on average 14 painful procedures per day during the first two weeks of life with fewer than 35 percent receiving appropriate analgesic therapy.

"While such surgical procedures in preterm infants are clearly necessary, the resulting pain and inflammation has been shown to lead to negative behavioral consequences later in life," Murphy said. "Our previous studies have shown that, just as in humans, neonatal inflammation in rodents (that did not receive preemptive pain medication) results in an increase in sensitivity to pain, stress, and decreased reaction to morphine as adults.

While evidence exists that morphine is efficacious in neonatal rodents, this is the first study to confirm the long-term behavioral benefits.

In this study, published online in *Pediatric Research*, a group of rat pups received an injection of morphine sulfate on the day of birth prior to inducing inflammation; another group received a saline injection instead. The groups were then raised identically and received identical procedures during a 60-day period. Rodents that received preemptive morphine behaved normally while those rats that received saline showed significant increases in pain sensitivity and were resistant to the pain relieving effects of morphine in adulthood.

"This tells us that morphine doesn't work very well in human children and adults that were formally in the NICU and didn't receive preemptive pain treatment, and since morphine is still the primary drug used to treat severe pain, this means that there is an entire subpopulation for which morphine doesn't work efficiently,"

Murphy said. "These results suggest that there are long-term benefits of providing all newborns with some sort of pain relieving medicine prior to the initiation of an invasive procedure."

*Murphy's work was supported by the National Institutes of Health, the Center for Behavioral Neuroscience, and the GSU Brains and Behavior Program.*

### **New evidence for homeopathy**

Two new studies conclude that a review which claimed that homeopathy is just a placebo, published in *The Lancet*, was seriously flawed.

George Lewith, Professor of Health Research at Southampton University comments: 'The review gave no indication of which trials were analysed nor of the various vital assumptions made about the data. This is not usual scientific practice. If we presume that homeopathy works for some conditions but not others, or change the definition of a 'larger trial', the conclusions change. This indicates a fundamental weakness in the conclusions: they are NOT reliable.'

The background to the ongoing debate is as follows:

In August 2005, *The Lancet* published an editorial entitled 'The End of Homeopathy', prompted by a review comparing clinical trials of homeopathy with trials of conventional medicine. The claim that homeopathic medicines are just placebo was based on 6 clinical trials of conventional medicine and 8 studies of homeopathy but did not reveal the identity of these trials. The review was criticised for its opacity as it gave no indication of which trials were analysed and the various assumptions made about the data.

Sufficient detail to enable a reconstruction was eventually published and two recently published scientific papers based on such a reconstruction challenge the *Lancet* review, showing that:

- \* Analysis of all high quality trials of homeopathy yields a positive conclusion.
- \* The 8 larger higher quality trials of homeopathy were all for different conditions; if homeopathy works for some of these but not others the result changes, implying that it is not placebo.
- \* The comparison with conventional medicine was meaningless.
- \* Doubts remain about the opaque, unpublished criteria used in the review, including the definition of 'higher quality'.

The *Lancet* review, led by Prof Matthias Egger of the Department of Social and Preventive Medicine at the University of Berne, started with 110 matched clinical trials of homeopathy and conventional medicine, reduced these to 'higher quality trials' and then to 8 and 6 respectively 'larger higher quality trials'. Based on these 14 studies the review concluded that there is 'weak evidence for a specific effect of homeopathic remedies, but strong evidence for specific effects of conventional interventions'.

There are a limited number of homeopathic studies so it is quite possible to interpret these data selectively and unfavourably, which is what appears to have been done in the *Lancet* paper. If we assume that homeopathy does not work for just one condition (Arnica for post-exercise muscle stiffness), or alter the definition of 'larger trial', the results are positive. The comparison with conventional medicine was meaningless: the original 110 trials were matched, but matching was lost after they were reduced to 8 and 6. But the quality of homeopathic trials was better than conventional trials.

This reconstruction casts serious doubts on the review, showing that it was based on a series of hidden judgments unfavourable to homeopathy. An open assessment of the current evidence suggests that homeopathy is probably effective for a number of conditions including allergies, upper respiratory tract infections and 'flu, but more research is desperately needed. Prof Egger has declined to comment on these findings.

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### **Bush rushes through 'harmful' environment laws**

\* 14:19 03 November 2008 \* NewScientist.com news service

**\* New Scientist staff and Reuters**

As the US presidential candidates sprint toward the finish line, the Bush administration is also sprinting to enact environmental policy changes before leaving power. The rule changes include getting wolves off the Endangered Species List, allowing power plants to operate near national parks, relaxing regulations for factory farm waste and making it easier for mountaintop coal-mining operations. None have found much favour with environmental groups.

Even some free-market organisations have joined conservation groups to urge a moratorium on last-minute rules proposed by the Interior Department and the Environmental Protection Agency, among others. "The Bush administration has had eight years in office and has issued more regulations than any administration in history,"

says Eli Lehrer of the Competitive Enterprise Institute. "At this point, in the current economic climate, it would be especially harmful to push through ill-considered regulations."

The Bush team has urged that regulations be issued no later than Saturday, so they can be put in effect by the time George W. Bush leaves office on 20 January 2009.

### **Hard to undo**

If they are in effect then, it will be hard for the next administration to undo them, and in any case, this may not be the top priority for a new president, says Matt Madia of OMB Watch, which monitors the White House Office of Management and Budget through which these proposed regulations must pass.

"This is typical," Madia says of the administration's welter of eleventh-hour rules. "It's a natural reaction to knowing that you're almost out of power." According to Madia, industry is likely to benefit if Bush's rules on the environment become effective. Whether it's the electricity industry or the mining industry or the agriculture industry, this is going to remove government restrictions on their activity and in turn they're going to be allowed to pollute more and that ends up harming the public."

What is unusual is the speedy trip some of these environmental measures are taking through the process. For example, one Interior Department rule that would erode protections for endangered species in favour of mining interests drew more than 300,000 comments from the public, which officials said they planned to review in a week, a pace that Madia calls "pretty ludicrous."

Rules only go into effect 30 to 60 days after they are finalised, and if they are not in effect when the next president takes office, that chief executive can decline to put them into practice – as Bush did with many rules finalised at the end of the Clinton administration. White House spokesman Tony Fratto denied the Bush team was cramming these regulations through in a hasty push.

### **Left-handed people are more inhibited**

\* 18:06 03 November 2008 NewScientist.com news service

**\* Ewen Callaway**

Lefties face a daily battle with a world designed for right-handers. Now it seems that left-handed people face a similar struggle in the mental sphere: behavioural research suggests they are prone to inhibition and anxiety.

When about to do something, left-handers tend to dither, says Lynn Wright, a behavioural psychologist at the University of Abertay Dundee, UK, who led the study. "Right-handers tend to jump in a bit."

On tests of behavioural inhibition, 46 left-handed men and women scored higher than 66 right-handers. Women, too, tended to rack up higher scores on the tests of reticence.

Wright and her colleagues uncovered these predilections by giving subjects a behavioural test that gauges both personal restraint and impulsiveness, qualities which seem to emanate from opposite hemispheres of our brains.

Compared to right-handers, lefties and women were likelier to agree with statements such as, "I worry about making mistakes" and "Criticism or scolding hurts me quite a bit". All groups responded similarly to statements such as "I often act on the spur of the moment" and "I crave excitement and new sensations", Wright's team found. The results could be due to wiring differences in the brains of left-handers and right-handers, she says.

### **Research**

suggests that handedness is a matter of degree (see "Edinburgh handedness inventory"). But in left-handers the right half of the brain is dominant, and it is this side that seems to control negative aspects of emotion. In right-handers the left brain dominates.

"It's all relative, you see," says Philip Corr, a behavioural neuroscientist at Swansea University, UK, noting that the differences in the brains of left and right-handers are usually slight.

However, he says handedness is not so much a predictor of personality as a great way to understand how emotions are handled in our brains. "Although we may have a predisposition to an inhibition, that may encourage us during adulthood or childhood to develop coping strategies," he says. "It could act as a blessing." Wright, a lefty, agrees. "They [left-handers] like to colour-code things, they like to write lists, it's almost a way to alleviate their stress," she says, adding that she is the classic example of the things that she finds in her work - "which is frightening". *Journal reference: Personality and Individual Differences (DOI: 10.1016/j.paid.2008.08.019)*

### **Cloning 'resurrects' long-dead mice**

\* 22:00 03 November 2008 NewScientist.com news service

**\* Rachel Nowak**

Healthy mice have been cloned from cells from dead mice that had been frozen for 16 years, raising the possibility that endangered species could be cloned from old carcasses that have been tossed in freezers, rather than from living cells frozen using elaborate techniques.

The finding also raises hopes of one day being able to resurrect extinct animals frozen in permafrost, such as the woolly mammoth, says Teruhiko Wakayama of the RIKEN Center for Developmental Biology in Kobe,

Japan, who led the research. "It would be very difficult, but our work suggests that it is no longer science fiction," he says.

The Wakayama team used a modified version of a cloning technique in which the nucleus of a mouse cell – in this case a cell from dead tissue that has been frozen and then thawed – is injected into a mouse egg that has had its nucleus removed. The resulting embryo was then used to create embryonic stem cells, capable of generating every cell type in the body, and the nuclei of these cells were injected into other eggs to produce clones.

In a surprise finding, the Wakayama team discovered that it was easiest to create clones from brain tissue, even though clones have never been created from living brain cells. Wakayama speculates that freezing and thawing the tissue somehow makes it easier to “reprogram” the brain cell nucleus. Brain tissue is also high in sugars, which can protect cells when they freeze. This may explain why the DNA remained undamaged, says Wakayama.

Other teams have already cloned mice from previously frozen dead cells. But this is the first time animals have been cloned from lumps of tissue frozen without the use of chemicals that might protect the cells from damage.

### **The gene bank in the freezer**

Globally, there are several cloning programmes that aim to increase the size of rapidly-dwindling populations of endangered species such as African wildcats, and maintain genetic diversity through one-off clonings of individuals that haven't bred. These programs depend on the animal cells undergoing specialised chemical procedures before being frozen so that they come to life when thawed.

Many zoos are not in a position to collect cells and freeze them in such a way as to preserve their viability, says Robert Lanza of Advanced Cell Technology in Worcester, Massachusetts, but they can put a dead animal "in a plastic bag and throw it in the freezer", he adds. "With a kitchen freezer you could store the genetic diversity of every panda in existence."

Despite the excitement surrounding the technique, more research will be needed before it can be used on endangered species, says Martha Gomez of the Audubon Nature Institute in New Orleans, Louisiana. "For instance, we don't know how long we can keep bodies of different species frozen and still get viable DNA. It may depend on size and species," she says.

What's more, most conservationists agree that cloning should be considered only as a last resort for species such as the northern white rhino, where all other attempts at conservation have failed, says Paul Bartels, manager of BioBankSA at the National Zoological Gardens of South Africa in Pretoria. Nonetheless, he says, he will be asking biologists to start freezing the bodies of endangered species that have died.

"We intend to bring this [finding] to the attention of as many biologists working on endangered species as possible, through circulars, e-mail, newsletters, and talks," he says.

### **A mammoth challenge**

Resurrecting extinct animals would be far trickier. Woolly mammoth carcasses would most likely have frozen and thawed several times over the aeons, which would cause far more damage to the nucleus than a one-off freezing.

Potentially easier would be cloning cryogenically frozen humans, though the consensus among cloning experts is that it would be unethical and dangerous to clone a human. In any case, people who sign up to be cryogenically preserved usually hope to be resuscitated rather than cloned.

*Journal reference: Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.0806166105*

## **Golf secret not all in the wrists**

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

After decades of research, the world may be closer to the perfect golf swing. The key, according to University of Surrey engineer Robin Sharp, is not to use full power from the start, but to build up to it quickly. Surprisingly, the wrists do not play a critical role in the swing's outcome, according to the new model. The analysis also shows that while bigger golfers might hit the ball further, it is not by much.

Any golfer will tell you that the idea of swinging harder to hit farther is not as straightforward as it might seem; the new results indicate that how - and when - the power develops is the key to distance.

### **Tricky balance**

Professor Sharp's work is based on a little-used model in which a golfer employs three points of rotation: the shoulders relative to the spine, the arms relative to the shoulders and the wrists relative to the arms.

Conventional wisdom has it that the timing of these rotations relative to one another is the key to a long drive. However, the new research, reported in the journal *Proceedings of the Royal Society*, is the first to optimise those timings and how the power of a swing is developed as they play out.

Prior models assumed one of two things: that the torque - the power in rotation - was applied at its maximum from the backswing, or that it ramped up throughout the swing, reaching its maximum at the point of impact.

Professor Sharp used a computer model first to fit to the swing styles of three professionals whose swings were measured with high-speed photography in 1968: Bernard Hunt, Geoffrey Hunt and Guy Wolstenholme.

The model showed that the club-head speed, and thus drive distance, of these professionals could have been improved by increasing the torque quickly to the maximum value and maintaining it throughout the rest of the swing. It is a delicate balance, however, and Sunday duffers may find it hard to implement Professor Sharp's prescription. "Generating too much arm speed too soon causes an early release, with the club-head reaching its maximum speed before it arrives at the ball," he says.

The key, Professor Sharp explains, is timing which torques are applied and when. And contrary to the old saying, it is not "all in the wrists". "In the expert swings studied, control of the arms and not the wrists appears to be the priority. "The optimal strategy consists of hitting first with the shoulders while holding back with arms and wrists and, after some delay, hitting through with the arms. At release, the wrists should hit through."

The model also shows that height is not much of an advantage in a long-distance shot. "A 21% bigger player can be expected to have just a 10% advantage in club-head speed," Professor Sharp said, which accounts for the fact that "good little ones are often not so far behind good big ones".

### **Put into practice**

Another person who is familiar with the swings of professional golfers is Simon Wickes, operations manager and biomechanics consultant for the Human Performance facilities at QinetiQ.

In the company's Biomechanics lab, visitors don a tight-fitting suit covered with reflectors that are tracked by 12 infrared-sensing cameras.

By tracking the independent motions of all the limbs and the club itself, the team can analyse in detail any number of motions, including golf swings; and the lab has been visited by professionals Nick Faldo and Justin Rose. "We're not golf pros," Mr Wickes explained. "We just show them where we think the problems are occurring. "What we were seeing with Justin Rose was the club head and the arms leading the body, rather than the shoulders leading the arms," he said.

It turns out that this reporter too had a problem of stiffness that makes the club lead the body. "It's something we've seen with other amateurs," Mr Wickes said after an analysis of my swing. "There's this feeling of trying to keep everything in alignment and by doing that you stiffen up because you don't want to have the variability you get if you loosen up your grip and loosen joints."

Useful though it is to know Professor Sharp's result, the perfect swing is not just a matter of the mechanics.

### **Drug mimics low-cal diet to ward off weight gain, boost running endurance**

A drug designed to specifically hit a protein linked to the life-extending benefits of a meager diet can essentially trick the body into believing food is scarce even when it isn't, suggests a new report in the November Cell Metabolism.

The drug called SIRT1720, which acts through the protein SIRT1, enhances running endurance in exercised mice and protects the animals against weight gain and insulin resistance even when they eat a high-fat diet, the researchers report. The drug works by shifting the metabolism to a fat-burning mode that normally takes over only when energy levels are low.

The findings bolster the notion that SIRT1 may be a useful target in the fight against metabolic disorders, including obesity and type 2 diabetes. It also helps lay to rest a long-standing controversy in the scientific world over the metabolic benefits of the red wine ingredient known as resveratrol. Resveratrol also acts on SIRT1, but its influence on other metabolic actors had left room to question exactly how it works.

" There has been a lot of controversy in the field about resveratrol action," said Johan Auwerx of Ecole Polytechnique Fédérale de Lausanne. "We find that the majority of the biology of resveratrol can be ascribed to SIRT1." While SIRT1 might not explain all of resveratrol's effects, the new results suggest that the central metabolic protein is responsible for about "80 percent of the picture," he said.

The researchers had conducted earlier studies to demonstrate many of the benefits of resveratrol. To further explore the underlying pathways responsible in the new study, they ran essentially the same experiments with the more potent and specific SIRT1-activating compound SIRT1720 developed by the company Sirtris Pharmaceuticals, Inc.

The researchers found that a low dose of SIRT1720 partially protected mice from gaining weight on a high-fat diet after 10 weeks of treatment. At higher doses, the drug completely prevented weight gain in the animals. SIRT1720 also improved blood sugar tolerance and insulin sensitivity and endowed the animals with greater athletic ability. " SIRT1720 made the animals run twice as long," Auwerx said. That improvement was seen

only when the researchers specifically exercised the animals. Their voluntary activity actually declined in the study as they hunkered down to save energy.

They found further evidence that the SIRT1 activator acts as a calorie-restriction mimetic that favors the use of fat stores by promoting the direct modification of multiple SIRT1 targets. It also induces chronic metabolic adaptations that involve the indirect activation of AMPK, an enzyme that regulates skeletal muscle glucose and the metabolism of fatty acids.

The major advantage of SRT1720 or any specific SIRT1 activator over resveratrol is that it is likely to come with fewer side effects, Auwerx said. That said, SRT1720 does have some limitations, Auwerx noted, in that the effects they observed came only at fairly high doses. He speculates that SRT1720 derivatives might get around this potential stumbling block for the drug's therapeutic promise. While the researchers did not observe any significant side effects of the drug in their study, they said further studies are needed to adequately address that question.

*The researchers include Jerome N. Feige, Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/Universite' Louis Pasteur, Illkirch, France; Marie Lagouge, Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/Universite' Louis Pasteur, Illkirch, France; Carles Canto, Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/Universite' Louis Pasteur, Illkirch, France; Axelle Strehle, Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/Universite' Louis Pasteur, Illkirch, France; Sander M. Houten, University of Amsterdam, Amsterdam, The Netherlands; Jill C. Milne, Sirtris Pharmaceuticals Inc., Cambridge, MA; Philip D. Lambert, Sirtris Pharmaceuticals Inc., Cambridge, MA; Chikage Mataka, Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/Universite' Louis Pasteur, Illkirch, France; Peter J. Elliott, Sirtris Pharmaceuticals Inc., Cambridge, MA; and Johan Auwerx, Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/Universite' Louis Pasteur, Illkirch, France, Institut Clinique de la Souris, Illkirch, France, Institute of Bioengineering, Ecole Polytechnique Federale de Lausanne (EPFL), Lausanne, Switzerland.*

### Death by hyperdisease

#### **How DNA detective work explains the extinction of Christmas Island's native rats**

It took less than a decade for native rats to become extinct on the Indian Ocean's previously uninhabited Christmas Island once Eurasian black rats jumped ship onto the island at the turn of the 20th century. But this story is more than the typical tale of direct competition: according to new genetic research published in PLoS One on November 5, black rats carried a pathogen that exterminated two endemic species, *Rattus macleari* and *R. nativitatis*. This study is the first to demonstrate extinction in a mammal because of disease, supporting the hypothesis proposed a decade ago that "hyperdisease conditions"—unusually rapid mortality from which a species never recovers—can lead to extinction.



***Rattus nativitatis* went extinct on Christmas Island by 1908.** P. Wynne/patriciawynne.com

"This study puts into play pathogenic organisms as mediators of extinction," says Alex D. Greenwood of the Biological Sciences Department at Old Dominion University in Norfolk, Virginia, and the Division of Vertebrate Zoology at the American Museum of Natural History. "Our study is the first to correlate a pathogen with an extinction event in mammals, although we know about disease-associated extinction in snails and disease-associated population declines in amphibians."

Black rats were introduced to Christmas Island via the S.S. Hindustan in 1899. A parasitologist noted a few years later that fleas on these rats carried a pathogenic protozoan related to the same organism that causes sleeping sickness in humans. The black rats were well adapted to this protozoan, known as *Trypanosoma lewisi*, but quite clearly, *R. macleari* and *R. nativitatis* were not. The native species were soon seen staggering around on footpaths, evidently very ill, and by 1908 it was clear to biologists on the island that both were extinct. Extinction of island-bound mammals is not uncommon: more than 80% of the mammals that have gone extinct in the last 500 years hailed from islands.

Although the parasitologist's findings have occasionally been cited in the specialist literature, scientists have been unable to agree that disease—rather than hybridization or competition between rat species—was the actual culprit. Greenwood and colleagues used ancient DNA procedures to determine if a rat-specific trypanosome could be detected in Museum samples and if trypanosomiasis could have caused the extinction of these species. The team collected samples from 21 specimens (virtually all extant) to see if the infectious agent existed in the population before and after contact with black rats. None of the three pre-contact samples were infected with the protozoan, but six of the 18 post-contact samples were infected. This suggests a very high rate of infection. Results were confirmed by sending a subset of the samples to a laboratory at the University of Copenhagen in

Denmark for independent testing. Finally, the group investigated the possibility of hybridization by testing for the distinctive genomes of the native rats in black rat species, but no evidence of this was found.

"This is not a case of humans over-hunting - I don't think anyone was that hungry," says Ross MacPhee, a Curator of Vertebrate Zoology at the American Museum of Natural History who proposed "hyperdisease conditions" as a mediator of extinction in 1997. "Within nine years of contact, these abundant, endemic species were evidently completely knocked out by an introduced disease—nothing else was around at the time that could have done the job. This study puts something else on the table as a reason for extinction."

The results of this study contrast with most scientists' view of the effect of pathogens on species. Most pathogens are self-limiting either because the disease burns itself out as the number of new hosts reduces, or because resistant individuals increase proportionally as susceptible individuals die out. Yet at least one mammalian species, the Tasmanian devil, shows every sign of undergoing a very severe collapse due to disease right now (in this case, from an apparently infectious form of cancer). At least a quarter of the total population has died out within the past decade, and some biologists predict the Tasmanian devil's extinction within a few years if the cancer continues to spread. Another famous Australian mammal, the Tasmanian tiger, or thylacine, is also thought to have suffered severe decline around 1910 because of disease, although the culprit has never been identified and interpretation of its final collapse is complicated by population decline due to bounty hunting.

"This study should get people to think about the spread of pathogen pollution," says Greenwood. "Pathogen pollution is the introduction of animal or plant diseases into a new environment. This pollution could affect many species that are in decline or in small numbers, ranging from accidental to active introduction like the building of Pleistocene Park in Russia or the repopulation of species for conservation purposes."

*The research in this paper was funded by The National Science Foundation. In addition to Greenwood and MacPhee, authors include Kelly Wyatt and Wayne Hynes of the Biological Sciences Department at Old Dominion University; Paula Campos and Thomas Gilbert of the Department of Biology at the University of Copenhagen; Sergios-Orestis Kolokotronis and Rob DeSalle of the Sackler Institute for Comparative Genomics at the American Museum of Natural History; and Peter Daszak of the Consortium for Conservation Medicine at the Wildlife Trust. To read the paper, visit <http://dx.plos.org/10.1371/journal.pone.0003602>.*

### **Vitamin B3 reduces Alzheimer's symptoms, lesions**

#### ***UC Irvine starts clinical trial on nicotinamide effect in Alzheimer's patients***

Irvine, Calif. — An over-the-counter vitamin in high doses prevented memory loss in mice with Alzheimer's disease, and UC Irvine scientists now are conducting a clinical trial to determine its effect in humans.

Nicotinamide, a form of vitamin B3, lowered levels of a protein called phosphorylated tau that leads to the development of tangles, one of two brain lesions associated with Alzheimer's disease. The vitamin also strengthened scaffolding along which information travels in brain cells, helping to keep neurons alive and further preventing symptoms in mice genetically wired to develop Alzheimer's.

"Nicotinamide has a very robust effect on neurons," said Kim Green, UCI scientist and lead author of the study. "Nicotinamide prevents loss of cognition in mice with Alzheimer's disease, and the beauty of it is we already are moving forward with a clinical trial." The study appears online Nov. 5 in the *Journal of Neuroscience*.

Nicotinamide is a water-soluble vitamin sold in health food stores. It generally is safe but can be toxic in very high doses. Clinical trials have shown it benefits people with diabetes complications and has anti-inflammatory properties that may help people with skin conditions.

Nicotinamide belongs to a class of compounds called HDAC inhibitors, which have been shown to protect the central nervous system in rodent models of Parkinson's and Huntington's diseases and amyotrophic lateral sclerosis. Clinical trials are underway to learn whether HDAC inhibitors help ALS and Huntington's patients.

In the nicotinamide study, Green and his colleague, Frank LaFerla, added the vitamin to drinking water fed to mice. They tested the rodents' short-term and long-term memory over time using water-maze and object-recognition tasks and found that treated Alzheimer's mice performed at the same level as normal mice, while untreated Alzheimer's mice experienced memory loss. The nicotinamide, in fact, slightly enhanced cognitive abilities in normal mice. "This suggests that not only is it good for Alzheimer's disease, but if normal people take it, some aspects of their memory might improve," said LaFerla, UCI neurobiology and behavior professor.

Scientists also found that the nicotinamide-treated animals had dramatically lower levels of the tau protein that leads to the Alzheimer's tangle lesion. The vitamin did not affect levels of the protein beta amyloid, which clumps in the brain to form plaques, the second type of Alzheimer's lesion.

Nicotinamide, they found, led to an increase in proteins that strengthen microtubules, the scaffolding within brain cells along which information travels. When this scaffolding breaks down, the brain cells can die. Neuronal death leads to dementia experienced by Alzheimer's patients.



"Microtubules are like highways inside cells. What we're doing with nicotinamide is making a wider, more stable highway," Green said. "In Alzheimer's disease, this highway breaks down. We are preventing that from happening."

*LaFerla and Green are affiliated with the Institute for Brain Aging and Dementia, which is conducting the clinical trial with funding from the Alzheimer's Association. The institute seeks volunteers who have been diagnosed with Alzheimer's, are 50 or older, and have a friend or relative who can accompany them to clinic visits and answer questions. Study participants will take the vitamin supplement or a placebo twice daily for 24 weeks, with seven visits to the UCI clinic. For more information on the clinical trial, contact Beatriz Yanez at 949-824-5733. UCI scientists Joan Steffan, Hilda Martinez-Coria, Xuemin Sun, Steven Schreiber and Leslie Thompson also worked on the study, which was supported in part by the Alzheimer's Drug Discovery Foundation and the National Institutes of Health.*

### **Mayo Clinic study finds risk of sudden cardiac death highest early after attack**

ROCHESTER, Minn. - People who survive a heart attack face the greatest risk of dying from sudden cardiac death (SCD) during the first month after leaving the hospital, according to a long-term community study by Mayo Clinic researchers of nearly 3,000 heart attack survivors. Sudden cardiac death can happen when the heart's electrical system malfunctions; if treatment - cardiopulmonary resuscitation and defibrillation - does not happen fast, a person dies. After that first month, the risk of sudden cardiac death drops significantly - but rises again if a person experiences signs of heart failure. The research results appear in the Nov. 5 edition of Journal of the American Medical Association.

#### **The Mayo Message**

This study emphasizes the need for physicians to stay in close contact with their heart attack patients, forming a partnership to recognize symptoms, says Veronique Roger, M.D., M.P.H., a Mayo Clinic cardiologist and lead author of the study. Physicians and patients - and their family members - need to be keenly alert for the symptoms of heart failure, as described by the American Heart Association, Dr. Roger says.

***Heart failure symptoms that require immediate attention include:***

- \* Shortness of breath***      ***\* Persistent cough or wheezing***
- \* Bloating and swelling***      ***\* Fatigue***      ***\* Confusion***

"There are three key findings here that can be immediately applied to heart attack patients today," Dr. Roger says. "One is that the first month post-heart attack is the highest risk period for patients to suffer sudden cardiac death - and acute surveillance is warranted. A second is that the risk drops rapidly after the first month, but this does not mean the patient is out of danger. Surveillance is still required after the first month because our third finding shows that even though the risk drops after the first month, the onset of symptoms of heart failure at any time after the heart attack markedly increases the risk of SCD."

#### **About the Study**

The study is one of the largest and longest comprehensive community studies performed by reviewing medical records. Drawing on data from the Rochester Epidemiology Project, the study analyzed the records of 2,997 men and women who had heart attacks in Olmsted County, Minn. - the county where Mayo Clinic is located - between 1979 and 2005. The patients' average age was 67 years. Patients were followed until death or the last recorded medical exam. Investigators were able to identify out-of-hospital deaths whose primary cause was listed as coronary heart disease. This enabled them to analyze sudden cardiac death trends. Housed at Mayo Clinic, the Rochester Epidemiology Project is one of the largest long-term, integrated databases of patient records in the world.

#### **Success of Secondary Prevention**

Another major finding of this study identifies a long-term, positive trend in the reduction of sudden deaths by nearly 40 percent over this time. This reflects medical advances in the care of heart patients, Dr. Roger says. These include the use of rapid restoration of blood flow during the initial phase of the heart attack, treated by emergency care and the adoption of "secondary prevention" measures. These measures include diet and lifestyle changes, such as taking medications to lower cholesterol levels and blood pressure. The measures help keep heart disease from developing or progressing, Dr. Roger says.

***Collaboration and Support*** *The Mayo Clinic research team also includes Susan Weston; Bernard Gersh, M.B.Ch.B., D.Phil.; and Terry Therneau, Ph.D. Collaborating in the research was A. Selcuk Adabag, M.D., from the Veterans Affairs Medical Center in Minneapolis. Their work was funded by the U.S. Public Health Service, the National Institutes of Health, and the Veterans Affairs Clinical Science Research & Development Service.*

### **Coral reefs found growing in cold, deep ocean**

Imagine descending in a submarine to the ice-cold, ink-black depths of the ocean, 800 metres under the surface of the Atlantic. Here the tops of the hills are covered in large coral reefs. NIOZ-researcher Furu Mienis studied the formation of these unknown cold-water relatives of the better-known tropical corals.

Furu Mienis studied the development of carbonate mounds dominated by cold-water corals in the Atlantic Ocean at depths of six hundred to a thousand metres. These reefs can be found along the eastern continental slope from Morocco to Norway, on the Mid-Atlantic Ridge and on the western continental slope along the east coast of Canada and the United States. Mienis studied the area to the west of Ireland along the edges of the Rockall Trough.

In her research Mienis analysed environmental factors like temperature, current speed and flow direction of seawater as these determine the growth of cold-water corals and the carbonate mounds. The measurements were made using bottom landers, observatories placed on the seabed from the NIOZ oceanographic research vessel 'Pelagia' and brought back to the surface a year later.

### **Food highways down to the deep**

Cold-water corals are mainly found on the tops of carbonate mounds in areas where the current is high due to strong internal waves. These waves are caused by tidal currents and lead to an increase in local turbulence that results in the seawater being strongly mixed in a vertical direction. The outcome is the creation of a kind of highway between the nutrient-rich, sunlit zone at the sea surface and the deep, dark strata where the 380 metre-high tops of the mounds are found. This allows the cold-water corals to feed on algae and zooplankton that live in the upper layers of the sea. *Lophelia pertusa* and *Madrepora oculata* are the most important coral species found on the European continental slopes.

### **Carbonate mounds**

How the carbonate mounds were formed was investigated by using a piston core from the research vessel to take samples of up 4.5 metres of sediment. These cores were then cut into thin slices that were analysed separately; the deeper the layer, the older the sediment. The samples studied were aged up to 200,000 years old. Large hiatuses found in the core were possibly caused by major changes in tidal currents. The groups of carbonate mounds develop in the direction of the strongest current and their tops are of equal height. The mounds were found to be built up from carbonate debris and sediment particles caught in between coral branches. These cold-water coral reefs have, therefore, not developed as a result of leakage of natural gas from the sea bed. However, that may well be the case in the Gulf of Mexico. This area is currently being studied from the American research vessel 'Nancy Foster' by Furu Mienis, her supervisor Tjeerd van Weering and NIOZ associate researcher Gerard Duineveld.

### **Threats**

Climate change has exerted a considerable influence on the growth of corals and the development of carbonate mounds. For example, corals stopped growing during ice ages. Present-day global warming and the resulting acidification of the oceans also pose a threat: organisms are less effective at taking up carbonate from seawater that is too acidic. This is true not only for corals but also for some species of algae that are a source of food for the corals. Other activities on the seabed that can cause damage to the coral reefs are offshore industries and bottom trawlers. A number of European areas containing cold-water coral reefs have thankfully already obtained protected status.

*This research was funded by the Netherlands Organisation for Scientific Research (NWO) and the European Science Foundation (ESF).*

### **Chicken genome plucked bare by inbreeding**

\* 12:42 04 November 2008 \* NewScientist.com news service

\* **Debora MacKenzie**

Modern livestock is bred to be super-productive. But at what cost? In the first genetic assessment of an entire agricultural product, scientists have found that, on average, super-productive modern chickens have lost more than half the genes present in ancestral populations. Some have lost 90%. This means most of the world's chickens lack characteristics that evolved when they lived in the wild, and may be useful again to help them face stress and disease as livestock.

Scientists want to breed DNA for traits such as disease resistance, or "animal well-being", back into commercial birds without introducing undesirable traits at the same time. Inbreeding is a concern with chickens, as the industry is dominated by a few big corporations that produce billions of birds from a handful of private breeding lines.

### **Homogenised hens**

Bill Muir of Purdue University in West Lafayette, Indiana, and colleagues used the recently sequenced chicken genome to measure genetic diversity across these lines, and compared it with 19th century breeds and wild chickens. They found that chickens had already lost a lot of genetic diversity before modern breeders got started.

In the 19th century, breeders turned the common European chicken – variably coloured birds with erratically shaped combs that periodically laid clutches of green speckled eggs – into breeds such as the White Leghorn.

These were white birds with identical combs that laid a single white egg daily. "The basic level of inbreeding was already 10% when modern poultry companies came into being," Muir told *New Scientist*.

### **Closer than auntie**

That means 10% of the genes of any two birds from the four classic breeds that were adopted by modern producers are already identical. Commercial breeding has pushed this commonality to 15% over the whole industry. That makes any two chickens more closely related than aunts and nieces in a typical human population, who on average share 12.5% of their genes. Most of the remaining genetic differences are between different companies' breeding lines, which never cross. Within lines, though, much more has been lost. Lines of chickens bred for eating share at least 30% of their genes. Some lines of laying hens share a staggering 90% of genes – meaning they have also lost 90% of their potential diversity.

Muir is heading an effort to reintroduce ancestral genes into modern chickens.

*Journal reference: Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.0806569105*

### **Precipitation levels may be associated with autism**

Children living in counties with higher levels of annual precipitation appear more likely to have higher prevalence rates of autism, according to a report in the November issue of *Archives of Pediatrics & Adolescent Medicine*, one of the *JAMA/Archives* journals. The results raise the possibility that an environmental trigger for autism may be associated with precipitation and may affect genetically vulnerable children.

In the past 30 years, autism rates have increased from approximately one in 2,500 to one in 150 children, according to background information in the article. Some of the increase is likely due to more active monitoring and changes in diagnostic criteria. "Nevertheless, the possibility of a true increase in prevalence cannot be excluded," the authors write. "Despite the increase in prevalence and the resulting increased attention paid to the condition, knowledge about what causes autism is limited. It is understood that biological factors play an important role, but environmental triggers may also be important."

Michael Waldman, Ph.D., of Cornell University, Ithaca, N.Y., and colleagues obtained autism prevalence rates from state and county agencies for children born in California, Oregon and Washington between 1987 and 1999. Using daily precipitation reports from the National Climatic Data Center, they calculated average annual rainfall by county from 1987 through 2001—which spans the dates when the children were school-aged.

"Autism prevalence rates for school-aged children in California, Oregon and Washington in 2005 were positively related to the amount of precipitation these counties received from 1987 through 2001," the authors write. "Similarly, focusing on Oregon and California counties with a regional center, autism prevalence was higher for birth cohorts that experienced relatively heavy precipitation when they were younger than 3 years." This corresponds to the time at which autism symptoms usually appear and when any post-natal environmental factors would be present.

Several potential explanations exist for the positive association, the authors note. Precipitation may be associated with more indoor activities, such as television and video viewing, that affect behavioral and cognitive development. The increased amount of time spent indoors also may expose children to more harmful chemicals, such as those in cleaning products, or decrease their exposure to sunshine, which helps the body produce vitamin D. "Finally, there is also the possibility that precipitation itself is more directly involved," the authors write. "For example, there may be a chemical or chemicals in the upper atmosphere that are transported to the surface by precipitation."

Because there is no direct clinical evidence of an environmental trigger for autism that is associated with precipitation, the results are preliminary, the authors note. However, "further research focused on establishing whether such a trigger exists and on identifying it is warranted," they conclude.

*(Arch Pediatr Adolesc Med. 2008;162[11]:1026-1034. Available pre-embargo to the media at [www.jamamedia.org](http://www.jamamedia.org).)*

**Editor's Note:** This study was supported by unrestricted research grants from Cornell University. Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

### **Editorial: Findings Tentative but Worth Publishing**

"As Waldman et al indicate, one can conceive that precipitation or its consequences (such as increased television watching, reduced vitamin D levels and enhanced exposure to indoor chemicals) might increase the incidence of autism," writes Noel S. Weiss, M.D., Dr.P.H., of the University of Washington, Seattle, in an accompanying editorial. "However, there are other possible explanations for the association with precipitation that they have observed."

"First, the criteria used to diagnose autism, and the completeness with which such diagnoses are identified by state agencies and regional centers, likely vary to a considerable extent across counties," Dr. Weiss continues. "Second, as is true in many cross-population comparisons, there may be unmeasured correlates of precipitation—beyond the consequences of precipitation—that bear on the occurrence of autism that themselves differ across counties."

"Of course, if a study's findings are no more than tentative ones—certainly, those of Waldman et al must be viewed as tentative—responsible authors will stress this," Dr. Weiss concludes. "In this instance, I believe that Waldman et al have indeed reported their results responsibly. They have made it clear that the message the public should take from their data regarding precipitation and autism is the same one suggested by an editorialist commenting on a recently observed modest association between prenatal exposure to cell phone use and behavior problems in childhood: 'No call for alarm, stay tuned'."

*(Arch Pediatr Adolesc Med. 2008;162[11]:1095-1096. Available pre-embargo to the media at [www.jamamedia.org](http://www.jamamedia.org).)*

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

### **Comment: When not to write about autism**

\* 18:26 04 November 2008 \* NewScientist.com news service

\* **Ewen Callaway**

USA Today heads its story: Study: Counties with more rainfall have higher autism rates. The BBC has Rainfall autism theory suggested, while The Daily Telegraph opts for Heavy rainfall could be linked to autism, scientists claim. These were some of the headlines in stories reporting a paper from scientists at Cornell University showing that between 1987 and 1999, counties in Washington, Oregon and California that got more rain had more cases of autism.

There is no claim that rain causes autism, and the authors are exceedingly conservative in making the connection. They argue that some unknown environmental factor related to precipitation or accompanying behaviour might contribute to autism.

To be fair, the sources mentioned above managed to keep sensationalism to a minimum, but others were not so restrained.

The Palm Beach Register, for example, had a Milli Vanilli-inspired headline as lame as it is misleading: "Autism: Blame it on the rain". Its opening line goes as far as to mention the discredited link between autism and a mercury preservative used in some childhood vaccines.

#### **Misleading the public?**

But should the story have been reported in the mainstream media at all? It offers nothing useful for the general public, parents, and even physicians. And press reports, blogs and other accounts of the study could even mislead the public.

I spoke with the study's lead author Sean Nicholson of Cornell last week. He is an insightful economist, and he carefully went over his team's data and its limitations with me.

His team accounted for some variables that might confound an association between autism and precipitation, and they back their claims up with impressive statistics.

They also underscore the speculative nature of the connection between autism rates and rainfall throughout the manuscript, which took a year and a half to get published.

#### **Unclear links**

But, Noel Weiss an epidemiologist at the University of Washington in Seattle who wrote an editorial on the paper – with the peculiar title Do These Results Warrant Publication? – makes an important point in answering "yes" to his rhetorical question:

"The authors' analysis and the editor's decision to publish it are to be lauded, despite the uncertain ultimate contribution of this work and the possibility (likelihood?) that non-professionals are going to misinterpret and misuse it."

The paper, he writes, is best digested by other epidemiologists, who may use the results to design trials that address potential links to autism that could be related to precipitation and related behaviour, such as lack of vitamin D exposure.

"Hopefully someone will be inspired to do a study that will be more direct and ultimately more persuasive for clinicians," Nicholson agrees.

Most media reports mention vitamin D and other "theories" – TV, household chemicals, and computer games – and the need for follow-up research to confirm these links.

Yet few reports say that these studies likely won't pan out under the microscope of well-designed clinical trials. Nor do they mention the importance of studying individuals with autism, rather than county-wide records, to gain true insight into a potential cause. This is epidemiology 101.

#### **Skip the story**

It's unrealistic to expect reporters to always wait for such confirmation before reporting on a study, especially one so tantalising.

An inevitable part of science and medical writing is covering research that others will eventually discredit. It's nearly impossible to determine what will stand the test of time – especially under deadline.

However, irresponsible reporting of the unproven link between autism and vaccines probably led some parents to pursue unproven and potentially dangerous chelation therapies for their kids, or to miss out on protective vaccines.

I can see worried parents hearing about the rain association, second- or third-hand, and keeping their kids in on showery days, or forcing them to play in the rain, or whatever "news you can use" suggestion gets tagged on to these stories.

For this reason, and it might be idealistic, but I think reporters and editors should have taken a pass on this story. There must have been a story on the benefits of broccoli out there.

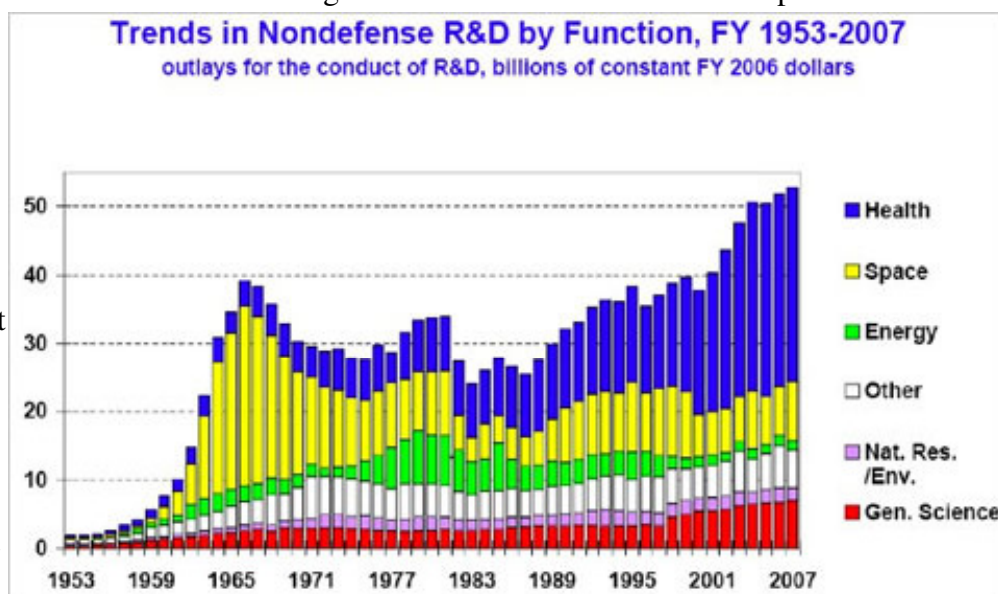
*Journal reference: Archives of Pediatrics and Adolescent Medicine (vol 11, p 1026)*

## What Would an Energy 'Moon Shot' Look Like?

By Andrew C. Revkin

This is a quick addendum to the previous post exploring what it would take for a president to pursue meaningful climate and energy policy in a multitasked world. One approach, hinted at by Senator Barack Obama off and on, is an Apollo-scale investment in advanced energy technology. The chances of a quick push of this sort are poor given the state of the economy, but what would a "Moon shot" for energy look like?

One way to consider the question is to look back at the gush of federal research and development dollars that underpinned the actual space race (and led to a string of innovations that NASA says have produced far greater economic benefits than the research cost). The graph above, generated a couple of years ago by Kei Koizumi at the American Association for the Advancement of Science, provides a hint. The yellow band in the graph is, in essence, a portrait of the space race as reflected in federal money for basic R&D related to going into orbit and to the Moon. (The purple band is essentially the war on cancer and similar health research. Military research, at \$75 billion a year, doesn't fit in this graph.)



**R&D spending**The space race was accompanied by a huge burst of federal research — the yellow band. What would an energy quest look like? (American Association for the Advancement of Science)

The green band is a half-century of federal investment in energy research. And that's not just renewable energy like solar power, but research in all energy sectors. To me, the energy graph resembles an emaciated python that had one decent meal. The bulge in the 1970s reflects the burst of interest in new energy technologies triggered by the oil shocks in that decade. President Ronald Reagan has been widely blamed for eviscerating energy research, but you can see in the graph that no subsequent administration or Congress took energy innovation seriously (and private-sector research investments have dropped even more).

These data are compiled annually by Mr. Koizumi and the science group's R&D budget and policy program. Tune in next year to see if that green line budges.

### Global Update

## Deadly New Virus Thought to Be Contained

By DONALD G. MCNEIL JR

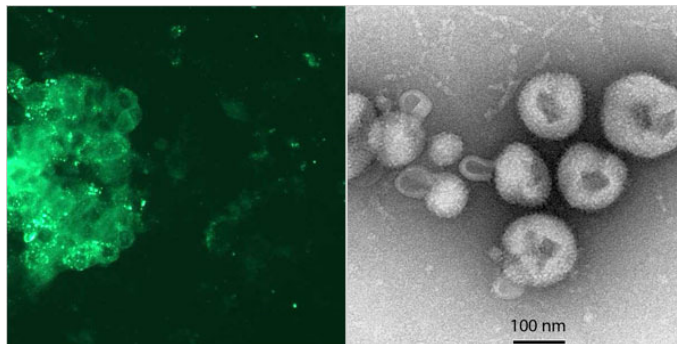
A new virus that causes fatal hemorrhagic fevers has been discovered in southern Africa. It killed four people in South Africa and sickened a fifth, but health authorities believe the outbreak has been contained.

The virus is a member of the arenavirus family, which also includes the causes of Lassa fever in West Africa and several South American fevers. While new viruses are often found in animals — a new blue-tongue virus was found in Swiss goats last month, for example — it is relatively rare to discover one fatal to humans, like the SARS coronavirus in 2002 or the sin nombre hantavirus in 1993.

How the first victim was infected is unknown, but arenaviruses are common in rodents; their dried urine, inhaled while sweeping, can transmit infection.

Confirmation that it is a new virus was made by the National Institute for Communicable Diseases in South Africa and by the Centers for Disease Control and Prevention in Atlanta.

The first victim was Cecilia Van Deventer, a safari tour booker in Lusaka, Zambia, who fell ill on Sept. 2 and was airlifted to Johannesburg. She apparently infected Hannes Els, the paramedic who accompanied her, and Gladys Mthembu, a nurse tending her at the Morningside Medi-Clinic in a Johannesburg suburb. The fourth to die was Maria Mokubung, who cleaned the room where Ms. Van Deventer died on Sept. 14. According to South African news reports, the last death was originally misdiagnosed because the victim had tuberculosis and meningitis and was hemorrhaging and confused when her family sought medical care. A fifth victim, a nurse who cared for Mr. Els, was in critical condition but responded to early treatment with the antiviral drug Ribavirin.



*Cultures showing arenavirus, which claimed victims near Johannesburg.*

The disease progresses from flu symptoms to diarrhea and a measles-like rash and then to respiratory and circulatory collapse.

The authorities said they knew of no new cases but would wait until 21 days from the last infection to declare the outbreak over.

Disease detective work was difficult, South African news media said. Because Ms. Van Deventer feared needles, little blood was drawn from her in Zambia; also, her body was cremated before the alarm was raised. Tissue samples from later victims had to be taken carefully in a high-security laboratory that was under renovation and had to be reopened.

Arenaviruses are named for their round sandy granules; “arena” is Latin for sand. A name for the new virus is being debated; Zambian authorities do not want one that will hurt tourism.

According to a government news service, Zambia’s first response to the outbreak was to close its border with Congo, the former Zaire, where Ebola fever, which is not related, originated.

#### Findings

### Obama and McCain Walk Into a Bar ...

By JOHN TIERNEY

While Americans choose their next president, let us consider a question more amenable to science: Which candidate’s supporters have a better sense of humor? In strict accordance with experimental protocol, we begin by asking you to rate, on a scale of 1 (not funny at all) to 9 (hilarious) the following three attempts at humor:

A) *Jake is about to chip onto the green at his local golf course when a long funeral procession passes by. He stops in midswing, doffs his cap, closes his eyes and bows in prayer. His playing companion is deeply impressed. “That’s the most thoughtful and touching thing I’ve ever seen,” he says. Jake replies, “Yeah, well, we were married 35 years.”*

B) *I think there should be something in science called the “reindeer effect.” I don’t know what it would be, but I think it’d be good to hear someone say, “Gentlemen, what we have here is a terrifying example of the reindeer effect.”*

C) *If you saw two guys named Hambone and Flippy, which one would you think liked dolphins the most? I’d say Flippy, wouldn’t you? You’d be wrong, though. It’s Hambone.*

Those were some of the jokes rated by nearly 300 people in Boston in a recent study. (You can rate some of the others at TierneyLab, [nytimes.com/tierneylab](http://nytimes.com/tierneylab).) The researchers picked out a variety of jokes - good, bad, conventional, absurdist - to look for differences in reactions between self-described liberals and conservatives.

They expected conservatives to like traditional jokes, like the one about the golfing widower, that reinforce racial and gender stereotypes. And because liberals had previously been reported to be more flexible and open to new ideas, the researchers expected them to get a bigger laugh out of unconventional humor, like Jack Handey’s “Deep Thoughts” about the reindeer effect and Hambone.

Indeed, the conservatives did rate the traditional golf and marriage jokes as significantly funnier than the liberals did. But they also gave higher ratings to the absurdist “Deep Thoughts.” In fact, they enjoyed all kinds of humor more. “I was surprised,” said Dan Ariely, a psychologist at Duke University, who collaborated on the



study with Elisabeth Malin, a student at Mount Holyoke College. “Conservatives are supposed to be more rigid and less sophisticated, but they liked even the more complex humor.”

Do conservatives have more fun? Should liberals start describing themselves as humor-challenged? To investigate these questions, we need to delve into the science of humor (not a funny enterprise), starting with two basic kinds of humor identified in the 1980s by Willibald Ruch, a psychologist who now teaches at the University of Zurich.

The first category is incongruity-resolution humor, or INC-RES in humor jargon. It covers traditional jokes and cartoons in which the incongruity of the punch line (the husband who misses his wife’s funeral) can be resolved by other information (he’s playing golf). You can clearly get the joke, and it often reinforces stereotypes (the golf-obsessed husband).

Dr. Ruch and other researchers reported that this humor, with its orderly structure and reinforcement of stereotypes, appealed most to conservatives who shunned ambiguity and complicated new ideas, and who were more repressed and conformist than liberals.

The second category, nonsense humor, covers many “Far Side” cartoons, Monty Python sketches and “Deep Thoughts.” The punch line’s incongruity isn’t neatly resolved — you’re left to enjoy the ambiguity and absurdity of the reindeer effect or Hambone’s affection for dolphins. This humor was reported to appeal to liberals because of their “openness to ideas” and their tendency to “seek new experiences.”

But then why didn’t the liberals in the Boston experiment like the nonsense humor of “Deep Thoughts” as much as the conservatives did? One possible explanation is that conservatives’ rigidity mattered less than another aspect of their personality. Rod Martin, the author of “The Psychology of Humor,” said the results of the Boston study might reflect another trait that has been shown to correlate with a taste for jokes: cheerfulness.

“Conservatives tend to be happier than liberals in general,” said Dr. Martin, a psychologist at the University of Western Ontario. “A conservative outlook rationalizes social inequality, accepting the world as it is, and making it less of a threat to one’s well-being, whereas a liberal outlook leads to dissatisfaction with the world as it is, and a sense that things need to change before one can be really happy.”

Another possible explanation is that conservatives, or at least the ones in Boston, really aren’t the stiffs they’re made out to be by social scientists. When these scientists analyze conservatives, they can sound like Victorians describing headhunters in Borneo. They try to be objective, but it’s an alien culture.

The studies hailing liberals’ nonconformity and “openness to ideas” have been done by social scientists working in a culture that’s remarkably homogenous politically. Democrats outnumber Republicans by at least seven to one on social science and humanities faculties, according to studies by Daniel Klein, an economist at George Mason University. If you’re a professor who truly “seeks new experiences,” try going into a faculty club today and passing out McCain-Palin buttons.

Could it be that the image of conservatives as humorless, dogmatic neurotics is based more on political bias than sound social science? Philip Tetlock, a psychologist at the University of California, Berkeley, who reviews the evidence of cognitive differences in his 2005 book, “Expert Political Judgment,” said that while there were valid differences, “liberals and conservatives are roughly equally closed-minded in dealing with dissonant real-world evidence.”

So perhaps conservatives don’t have a monopoly on humorless dogmatism. Maybe the stereotype of the dour, rigid conservative has more to do with social scientists’ groupthink and wariness of outsiders — which, come to think of it, resembles the herding behavior of certain hoofed animals. Ladies and gentlemen, what we have here is a terrifying example of the reindeer effect.

### **'Junk' DNA proves functional**

#### ***Helps explain human differences from other species***

In a paper published in *Genome Research* on Nov. 4, scientists at the Genome Institute of Singapore (GIS) report that what was previously believed to be “junk” DNA is one of the important ingredients distinguishing humans from other species.

More than 50 percent of human DNA has been referred to as “junk” because it consists of copies of nearly identical sequences. A major source of these repeats is internal viruses that have inserted themselves throughout the genome at various times during mammalian evolution.

Using the latest sequencing technologies, GIS researchers showed that many transcription factors, the master proteins that control the expression of other genes, bind specific repeat elements. The researchers showed that from 18 to 33% of the binding sites of five key transcription factors with important roles in cancer and stem cell biology are embedded in distinctive repeat families.

Over evolutionary time, these repeats were dispersed within different species, creating new regulatory sites throughout these genomes. Thus, the set of genes controlled by these transcription factors is likely to significantly differ from species to species and may be a major driver for evolution.

This research also shows that these repeats are anything but "junk DNA," since they provide a great source of evolutionary variability and might hold the key to some of the important physical differences that distinguish humans from all other species.

The GIS study also highlighted the functional importance of portions of the genome that are rich in repetitive sequences.

"Because a lot of the biomedical research use model organisms such as mice and primates, it is important to have a detailed understanding of the differences between these model organisms and humans in order to explain our findings," said Guillaume Bourque, Ph.D., GIS Senior Group Leader and lead author of the Genome Research paper.

"Our research findings imply that these surveys must also include repeats, as they are likely to be the source of important differences between model organisms and humans," added Dr. Bourque. "The better our understanding of the particularities of the human genome, the better our understanding will be of diseases and their treatments."

"The findings by Dr. Bourque and his colleagues at the GIS are very exciting and represent what may be one of the major discoveries in the biology of evolution and gene regulation of the decade," said Raymond White, Ph.D., Rudi Schmid Distinguished Professor at the Department of Neurology at the University of California, San Francisco, and chair of the GIS Scientific Advisory Board.

"We have suspected for some time that one of the major ways species differ from one another – for instance, why rats differ from monkeys – is in the regulation of the expression of their genes: where are the genes expressed in the body, when during development, and how much do they respond to environmental stimuli," he added.

"What the researchers have demonstrated is that DNA segments carrying binding sites for regulatory proteins can, at times, be explosively distributed to new sites around the genome, possibly altering the activities of genes near where they locate. The means of distribution seem to be a class of genetic components called 'transposable elements' that are able to jump from one site to another at certain times in the history of the organism. The families of these transposable elements vary from species to species, as do the distributed DNA segments which bind the regulatory proteins."

Dr. White also added, "This hypothesis for formation of new species through episodic distributions of families of gene regulatory DNA sequences is a powerful one that will now guide a wealth of experiments to determine the functional relationships of these regulatory DNA sequences to the genes that are near their landing sites. I anticipate that as our knowledge of these events grows, we will begin to understand much more how and why the rat differs so dramatically from the monkey, even though they share essentially the same complement of genes and proteins."

**Research publication:**

*The research findings are published in the Nov. 4, 2008 issue of GENOME RESEARCH in paper titled, "Evolution of the mammalian transcription factor binding repertoire via transposable elements".*

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### **Genetic study provides new insights into molecular basis of language development**

Scientists have identified the first gene that is associated with a common childhood language disorder, known as specific language impairment (SLI). The gene – CNTNAP2 – has also been recently implicated in autism, and could represent a crucial genetic link between the two disorders.

Although most children acquire proficient spoken language almost automatically and with little conscious effort, a significant number develop unexplained difficulties in producing and understanding language. SLI is the most common such disorder, affecting up to 7% of pre-school children.

In a study published today in the New England Journal of Medicine, researchers at the Wellcome Trust Centre for Human Genetics, University of Oxford, discovered that particular variants of the CNTNAP2 gene were significantly associated with language deficits in a large sample of families with SLI.



"It has long been suspected that inherited factors play an important role in childhood language disorders," says Dr Simon Fisher, a Royal Society Research Fellow at the Wellcome Trust Centre, who led the research. "But this is the first time that we have been able to implicate variants of a specific gene in common forms of language impairment."

The trail to this new finding began with studies of another language-related gene, called FOXP2, previously found to be mutated in rare cases of a severe speech and language disorder. Versions of FOXP2 are found in many animals, including primates, birds, bats and mice. In birds, for example, it has been linked to song, in mice to learning of sequences of movement, and in bats it may relate to echo-location.

FOXP2 acts to regulate other genes in the brain, switching them on and off. Dr Fisher and colleagues began analysing human neurons grown in the laboratory in order to search for these target genes. They identified CNTNAP2 as a key part of the network.

When the scientists went on to investigate CNTNAP2 in 184 families with common language impairments, they found that children who carried certain variants of the gene displayed reduced language abilities, most strikingly for a measure of nonsense-word repetition that is known to be a strong indicator of SLI.

Recent studies have also implicated CNTNAP2 in autism, a syndrome characterised by communication deficits, impaired social interaction, and repetitive behaviours. In particular, one investigation uncovered an association between variants of CNTNAP2 and delayed language development in children with autism.

"Our findings suggest that similar changes in the regulation or function of this gene could be involved in language deficits in both SLI and autism," says Dr Fisher. "This supports the emerging view that autism involves the convergence of a number of distinct problems underpinned by different genetic effects."

Professor Dorothy Bishop, a Wellcome Trust Principal Research Fellow at the University of Oxford, who specialises in the study of children's communication impairments, comments: "All too often parents of language-impaired children are blamed for their children's difficulties, even though the evidence has been around for a while that genes are implicated. These are important yet neglected disorders that can have long term effects on educational and social outcomes. This landmark study provides an important first step in unravelling the complex biological factors that determine susceptibility to language difficulties."

It is not yet known exactly how changes to CNTNAP2 interfere with language development, but there are some tantalising clues. The gene makes a type of protein called a neurexin, which sits in the membranes of neurons, controlling interactions between different cells during the development and wiring up of the nervous system. In early development, the protein appears to be strongly expressed in parts of the human brain which go on to become important for language processing, such as the frontal lobes.

The researchers are now investigating whether variations in CNTNAP2 contribute to natural variation in linguistic abilities in the general population.

"Genes like CNTNAP2 and FOXP2 are giving us an exciting new molecular perspective on speech and language development, one of the most fascinating but mysterious aspects of being human," says Dr. Fisher "There are likely to be more answers buried in our genome. This work promises to shed light on how networks of genes help to build a language-ready brain."

### **Electron pairs precede high-temperature superconductivity**

***New method exploring 'energy gap' shows electron pairs exist before superconductivity sets in***

UPTON, NY - Like astronomers tweaking images to gain a more detailed glimpse of distant stars, physicists at the U.S. Department of Energy's (DOE) Brookhaven National Laboratory have found ways to sharpen images of the energy spectra in high-temperature superconductors - materials that carry electrical current effortlessly when cooled below a certain temperature. These new imaging methods confirm that the electron pairs needed to carry current emerge above the transition temperature, before superconductivity sets in, but only in a particular direction.

"Our findings rule out certain explanations for the development of superconductivity in these materials, and lend support to other, competing theories," said Brookhaven physicist Peter Johnson, leader of the group whose work is described in the November 6, 2008, issue of Nature. Honing in on the mechanism for high-temperature (high-T<sub>c</sub>) superconductivity may help scientists engineer new materials to make use of the current-carrying phenomenon in transformative applications such as high-efficiency transmission lines in the U.S. power grid.

Scientists already know that electrons in a superconducting material must pair up to carry the current. But whether these pairs form at or above the transition temperature has been a mystery, until now.

To search for pre-formed electron pairs, the Brookhaven team bombarded a copper-oxide material, held at temperatures above and below the transition temperature, with beams of light from the National Synchrotron Light Source, and analyzed the energy spectrum of electrons emitted from the sample. This method, known as angle-resolved photoemission spectroscopy (ARPES), ordinarily gives a clear picture of only half of the energy

spectrum - all the levels electrons can occupy below the so-called Fermi level. To glimpse the other half, above the Fermi level, the scientists employed methods of analysis similar to those used by astronomers to increase the resolution of celestial images.

"If you look through a telescope with poor resolution, you'll see the moon, but the stars are lost," Johnson said. "But if you improve your resolution you see the stars and everything else. By improving our resolution we can use ARPES to see the few electrons that occasionally occupy levels above the Fermi level. We have devised ways to sharpen our images so we can look at the weak signals from above the Fermi level in finer and finer detail."

Seeing both sides of the Fermi level is important because, when a material becomes a superconductor, there is an energy gap surrounding the Fermi level. A perfectly symmetrical gap - equally spaced above and below the Fermi level - is a strong indication that electrons are paired up. That superconducting gap exists at and below the transition temperature, as long as a material acts as a superconductor.

But Johnson's team and other scientists had previously observed a second gap, or pseudogap, in some high-T<sub>c</sub> materials, well above the transition temperature. If this pseudogap exhibited the same symmetry around the Fermi level, Johnson reasoned, it would be definitive evidence of paired electrons above the transition temperature. Using their new image-enhancing techniques, Johnson's team demonstrated that the pseudogap does indeed exhibit this same symmetry.

"We can now say for certain that electrons are forming pairs above the transition temperature, before the material becomes a superconductor," Johnson said.

The scientists made another interesting observation: The pairing occurs only along certain directions in the crystalline lattice of atoms making up the material - only along the directions in which copper atoms are bonded with oxygen atoms.

Together, the existence of preformed electron pairs and their directional dependence should help clarify the picture of high-T<sub>c</sub> superconductivity, Johnson said. For example, the findings rule out some theories to explain the high-T<sub>c</sub> phenomenon (e.g. certain "spin density wave" and "charge density wave" derived theories). But the new findings are consistent with theories that consider the pre-superconducting state to be derived from a "Mott insulator," as well as theories in which " [http://www.bnl.gov/bnlweb/pubaf/pr/PR\_display.asp?prID=06-57] charge stripes," previously discovered at Brookhaven Lab, might play a role in electron pairing.

"It's still a very complicated picture and one of the great mysteries of modern science," Johnson said. "With something like 150 theorists working in the field, we have 150 theories of how these materials work. But as we develop new techniques, we are making progress narrowing down the mechanism."

*This work was funded by the Office of Basic Energy Sciences within DOE's Office of Science.*

### **Friendly bacteria reduce hospital infections**

A probiotic bacterium, *Lactobacillus plantarum* 299, has been used to out-compete the dangerous bacteria that cause respiratory illness in ventilated patients. Research published in BioMed Central's open access journal *Critical Care* describes how applying a bacterial solution in place of normal antiseptics is effective in preventing the most common cause of ventilator-associated pneumonia (VAP).

Bengt Klarin from the University Hospital in Lund, Sweden, led a team of researchers who carried out a randomised, controlled trial in fifty patients, comparing friendly bacteria to the normally used antiseptic chlorhexidine (CHX). Klarin said, "We hypothesised that swabbing the mouth with probiotics would be an effective (and microbiologically attractive) method of reducing pathogenic oral microorganisms in intubated, mechanically ventilated, critically ill patients."

VAP is a common complication in patients on breathing machines. It occurs when harmful bacteria from the mouth, throat or breathing tube are inhaled into the lungs. Because most people on ventilation are sedated or unable to communicate, initial symptoms of pneumonia can be difficult to spot. According to Klarin, "VAP is connected with longer intensive care and hospital stays, additional costs and high mortality. The risk of developing this condition increases by 1% with each additional day of mechanical ventilation."

The authors found that the probiotic treatment was as effective as the antiseptic. Use of the bacteria has other advantages; there are common side effects associated with CHX use in oral care, including tooth discoloration, irritation and, very occasionally, serious allergic reactions. Moreover, CHX diluted by saliva and represents an additional risk for the creation of resistant strains. The authors claim that the *L. plantarum* 299 solves these problems, "It is not likely to incorporate resistance genes or plasmids or to transfer genetic material. Consequently it does not contribute to the development of antibiotic-resistant strains. As the bacteria adhere to the oral mucosa, they are able to counteract potentially pathogenic bacteria around the clock, which is superior to the fairly short-term effect of orally applied chemical agents."

*L. plantarum* is normally present in saliva and is also commonly found in fermented food products like pickles and sauerkraut. The authors found no negative side effects of using it in this study.

#### **Notes to Editors**

1. *Use of the probiotic Lactobacillus plantarum 299 to reduce pathogenic bacteria in the oropharynx of intubated patients: a randomised controlled open pilot study* Bengt Klarin, Göran Molin, Bengt Jeppsson and Anders Larsson *Critical Care (in press)*

### **Rocks could be harnessed to sponge vast amounts of CO<sub>2</sub> from air, says study** ***Proposed method would speed natural reactions a million times***

Scientists say that a type of rock found at or near the surface in the Mideast nation of Oman and other areas around the world could be harnessed to soak up huge quantities of globe-warming carbon dioxide. Their studies show that the rock, known as peridotite, reacts naturally at surprisingly high rates with CO<sub>2</sub> to form solid minerals - and that the process could be speeded a million times or more with simple drilling and injection methods. The study appears in this week's early edition of the *Proceedings of the National Academy of Sciences*.

Peridotite comprises most or all of the rock in the mantle, which undergirds earth's crust. It starts some 20 kilometers or more down, but occasionally pieces are exhumed when tectonic plates collide and push the mantle rock to the surface, as in Oman. Geologists already knew that once exposed to air, the rock can react quickly with CO<sub>2</sub>, forming a solid carbonate like limestone or marble. However, schemes to transport it to power plants, grind it and combine it with smokestack gases have been seen as too costly and energy intensive. The researchers say that the discovery of previously unknown high rates of reaction underground means CO<sub>2</sub> could be sent there artificially, at far less expense. "This method would afford a low-cost, safe and permanent method to capture and store atmospheric CO<sub>2</sub>," said the lead author, geologist Peter Kelemen.

Kelemen and geochemist Juerg Matter, both at Columbia University's Lamont-Doherty Earth Observatory, made the



***Large areas of Omani desert are covered with carbonate minerals that have reacted with bedrock.*** Lamont-Doherty Earth Observatory

discovery during field work in the Omani desert, where they have worked for years. Their study area, a Massachusetts-size expanse of largely bare, exposed peridotite, is crisscrossed on the surface with terraces, veins and other formations of whitish carbonate minerals, formed rapidly in recent times when minerals in the rock reacted with CO<sub>2</sub>-laden air or water. Up to 10 times more carbonates lie in veins belowground; but the subterranean veins were previously thought to be formed by processes unconnected to the atmosphere, and to be nearly as old as the 96-million-year-old rock itself. However, using conventional carbon isotope dating, Kelemen and Matter showed that the underground veins are also quite young— 26,000 years on average—and are still actively forming as CO<sub>2</sub>-rich groundwater percolates downward. Many underground samples were conveniently exposed in newly constructed road cuts. All told, Kelemen and Matter estimate that the Omani peridotite is naturally absorbing 10,000 to 100,000 tons of carbon a year—far more than anyone had thought. Similarly large exposures of peridotite are known on the Pacific islands of Papua New Guinea and Caledonia, and along the coasts of Greece and the former Yugoslavia; smaller deposits occur in the western United States and many other places.

The scientists say that the process of locking up carbon in the rocks could be speeded 100,000 times or more simply by boring down and injecting heated water containing pressurized CO<sub>2</sub>. Once jump-started in this way, the reaction would naturally generate heat—and that heat would in turn hasten the reaction, fracturing large volumes of rock, exposing it to reaction with still more CO<sub>2</sub>-rich solution. Heat generated by the earth itself also would help, since the further down you go, the higher the temperature. (The exposed Omani peridotite extends down some 5 kilometers.) The scientists say that such a chain reaction would need little energy input after it was started. Accounting for engineering challenges and other imperfections, they assert that Oman alone could probably absorb some 4 billion tons of atmospheric carbon a year—a substantial part of the 30 billion sent into the atmosphere by humans, mainly through burning of fuels. With large amounts of new solids forming underground, cracking and expansion would generate micro-earthquakes—but not enough to be readily perceptible to humans, says Kelemen.

"It's fortunate that we have these kinds of rocks in the Gulf region," said Matter. Much of the world's oil and gas is produced there, and Oman is constructing new gas-fired electric plants that could become large sources of CO<sub>2</sub> could be pumped down.

Matter has been working on a separate project in Iceland, where a different kind of rock, volcanic basalt, also shows promise for absorbing CO<sub>2</sub> produced by power plants. Trials there are set to begin in spring 2009, in partnership with Reykjavik Energy, and the universities of Iceland and Toulouse (France).

According to the scientists, Petroleum Development Oman, the state oil company, is interested in a pilot program. Kelemen said: "We see this as just one of a whole suite of methods to trap carbon. It's a big mistake to think that we should be searching for one thing that will take care of it all."

*The paper, "In situ carbonation of peridotite for CO<sub>2</sub> storage," is available at*

*<http://www.pnas.org/content/early/2008/10/31/0805794105.full.pdf+html> or from the scientists, or the Proceedings of the National Academy of Sciences press office: PNASnews@nas.edu or 202-334-1310.*

### **Minority patients discouraged from cancer screening by negative messages**

PHILADELPHIA – New behavioral science research published in *Cancer Epidemiology, Biomarkers & Prevention*, a journal of the American Association for Cancer Research, found that constantly emphasizing the negative consequences of a lack of cancer screening among minorities can actually make them less likely to go for screening.

"We have typically assumed that one of the best ways to motivate individuals is to point out disparities in health, but we may be having negative unintended consequences," said Robert Nicholson, Ph.D., an assistant professor in the Department of Neurology and Psychiatry at the St. Louis University School of Public Health. "Instead of motivating people who would be less likely to get these services in the first place, we may be driving them away."

Minority communities have been historically underserved by cutting edge medical efforts, and leaders in cancer and other health groups have tried to increase awareness and compliance with known prevention and treatment strategies. However, whether this communication was effective was not known.

Nicholson and colleagues conducted a double-blind, randomized trial among 300 African-American adults. The adults were asked to read one of four articles about colon cancer and then answer questions about their likelihood of getting screened.

The first article emphasized that colon cancer was an important problem for African-Americans. The second emphasized that outcomes for blacks with colon cancer were worse than for whites, while a third said that although outcomes for African-Americans were improving the improvement was less than seen among whites. Finally, a fourth article discussed how outcomes for blacks with colon cancer were improving over time.

If African-Americans read the article that said outcomes for blacks were improving over time, they were more likely to have a positive emotional response than if they read any of the other three articles. The article most likely to cause a negative response was the one that simply stated the problem.

Similarly, those that read the article about African-Americans making progress in outcomes for colon cancer were far more likely to want to be screened than those who read any of the other three articles.

The mean age of the participants was 54.4 years, 76 percent were women and 89 percent had completed high school. Comprehension analysis found that all participants understood what they had read.

Nicholson said they did not ask questions about motivation, but he suggests that a general mistrust of the medical community may be playing a role. If information reinforces that mistrust, then African-Americans are less likely to be screened.

"We believe that a positive message would go a long way toward overcoming mistrust," Nicholson said. "We need the right kind of message for the right kind of person, and not to assume that what we have always done is working."

### **XDR-TB: Deadlier and more mysterious than ever**

New research has found that XDR-TB is increasingly common and more deadly than previously known. Extensively drug-resistant tuberculosis (XDR-TB) is a growing public health threat that is only just beginning to be understood by medical and public health officials.

Patients with XDR-TB are four times as likely to fail treatment and three times more likely to die than patients with other forms of multi-drug-resistant TB (MDR-TB), according to a recent study that directly compared patients with XDR-TB to individuals with other types of MDR-TB to determine the differences in treatment outcomes and long-term survival rates. Researchers also found that MDR-TB was "a major threat to public health," representing 2.7 percent of new TB cases in South Korea in 2004, up from 1.6 percent in 1994.

The results were published in the second issue for November of the American Journal of Respiratory and Critical Care Medicine, a journal of the American Thoracic Society.

Since it appeared on the public health radar in 2006, XDR-TB rekindled an urgent interest in preventing, fighting and containing TB. But at the same time, little was known about how XDR-TB changed the face of combating TB on all fronts, from the perspective of the patient, the clinician and the public health official.

"Treatment outcomes [of XDR-TB] have varied among studies, and data on long-term survival are still scarce," wrote Tae Sun Shim, M.D., an associate professor at Asan Medical Center in Seoul, South Korea, and a principal investigator of the study. "[This] is the largest report that we know of that compares patients with XDR-TB with other patients with MDR-TB to determine the impact of XDR-TB on treatment outcomes and long-term survival in mostly HIV-negative patients with MDR-TB."

The study reviewed the medical records of more than 1,400 patients in South Korea with MDR-TB (which includes XDR-TB) from all national hospitals, Korean National TB Association chest clinics and select university hospitals. In addition to the patients' demographic information, their history of TB and previous treatments were noted with regard to outcome. In this study, XDR-TB was defined as MDR-TB resistant to both ofloxacin and at least one second-line injectable drug. The researchers found that patients with XDR-TB were significantly older than MDR-TB patients, were more likely to have a history of treatment with second-line TB drugs, and more likely to have a history of being treated for TB two or more times.

Among this population, treatment failure was, not surprisingly, much more common when compared to other patients with MDR-TB. While relapse rate among "cured" patients also tended to be higher among patients with XDR-TB, the difference was not statistically significant.

"[Having] XDR-TB was the strongest predictor of both all-cause and TB-related mortality, and survival curves showed higher cumulative mortality among patients with XDR-TB than in other patients with MDR-TB," wrote Dr. Shim. Over the three to seven years that the study's patient population was monitored, approximately 50 percent of those identified with XDR-TB died, which was a mortality rate similar to untreated TB patients in South India, and one that becomes even worse with HIV co-infection.

Perhaps the biggest public health threat associated with XDR-TB, however, is not its particular virulence, but the lack of information and treatment options that medical and public health officials have on which to draw. The collective dearth of knowledge was likened by Giovanni Battista Migliori, M.D., Morgan Richardson, R.N., P.H.N., and Christopher Lange, M.D., Ph.D., co-authors of the accompanying editorial, to the proverbial blind men trying to describe an elephant—too big a task to accomplish with too little information.

The risks of this lack of information are clear. "Regrettably, a new drug [to treat TB] has not been licensed in decades," they wrote, saying that only further research and concerted effort to understand and quantify the effects of the disease can really prevent MDR- and XDR-TB from becoming pandemic health crises.

"As we wait for new diagnostics and drugs that can meet the challenge of XDR-TB, we must work with what we presently have to create the optimal conditions for success and thus seize the opportunity we have to eliminate tuberculosis," they concluded. *Full text of original article available*

*here: <http://www.thoracic.org/sections/publications/press-releases/resources/XDR-TB%20111508.pdf>*

## **Silencing growth inhibitors could help recovery from brain injury**

### ***Small-molecule drugs could spark neuron regeneration***

Boston, MA—Silencing natural growth inhibitors may make it possible to regenerate nerves damaged by brain or spinal cord injury, finds a study from Children's Hospital Boston. In a mouse study published in the November 7 issue of *Science*, researchers temporarily silenced genes that prevent mature neurons from regenerating, and caused them to recover and re-grow vigorously after damage.

Because injured neurons cannot regenerate, there is currently no treatment for spinal cord or brain injury, says Zhigang He, PhD, Associate Professor of Neurology at Children's and senior author on the paper. Previous studies that looked at removing inhibitory molecules from the neurons' environment, including some from He's own lab, have found only modest effects on nerve recovery. But now He's team, in collaboration with Mustafa Sahin, MD, PhD, Assistant Professor of Neurology at Children's, demonstrates that re-growth is primarily regulated from within the cells themselves.

"We knew that on completion of development, cells stop growing due to genetic mechanisms that prevent overgrowth," explains He. "We thought that this kind of mechanism might also prevent regeneration after injury."

The key pathway for controlling cell growth in neurons, known as the mTOR pathway, is active in cells during development, but is substantially down-regulated once neurons have matured. Moreover, upon injury, this pathway is almost completely silenced, presumably for the cell to conserve energy to survive. He and colleagues reasoned that preventing this down-regulation might allow regeneration to occur.

He and his team used genetic techniques to delete two key inhibitory regulators of the mTOR pathway, known as PTEN and TSC1, in the brain cells of mice. After two weeks, the mice were subjected to mechanical damage of the optic nerve. Two weeks post-injury, up to 50 percent of injured neurons in the mice with gene deletions of PTEN or TSC1 survived, compared to about 20 percent of those without the deletions. And of the surviving mutant mice, up to 10 percent showed significant re-growth of axons, the fiber-like projections of neurons that transmit signals, over long distances. This re-growth increased over time.

Although this study used genetic techniques, He notes that it may be possible to accomplish the same re-growth through pharmacologic means. "This is the first time it has been possible to see such significant regeneration by manipulating single molecules," says He. "We believe that these findings have opened up the possibility for making small-molecule drugs or developing other approaches to promote axon regeneration."

While such long-distance regeneration of axons has not been seen before using other techniques, it is still unknown whether these regenerating axons can restore function, He adds.

The research group is now looking at axon regeneration after spinal cord injury and given the current availability of specific PTEN inhibitors, the researchers hope that these and similar small-molecule inhibitors of the mTOR pathway will lead to future neural regeneration therapies.

*Kevin Park, PhD, Kai Liu, PhD, Yang Hu, PhD, and Patrice Smith, PhD, all of Children's, share significant authorship of the paper. This study was supported by grants from the National Institute of Neurological Disorders and Stroke, Wings for Life, the Adelson Foundation and the Tuberous Sclerosis Alliance.*

## **Silencing growth inhibitors could help recovery from brain injury**

### ***Small-molecule drugs could spark neuron regeneration***

Boston, MA—Silencing natural growth inhibitors may make it possible to regenerate nerves damaged by brain or spinal cord injury, finds a study from Children's Hospital Boston. In a mouse study published in the November 7 issue of *Science*, researchers temporarily silenced genes that prevent mature neurons from regenerating, and caused them to recover and re-grow vigorously after damage.

Because injured neurons cannot regenerate, there is currently no treatment for spinal cord or brain injury, says Zhigang He, PhD, Associate Professor of Neurology at Children's and senior author on the paper. Previous studies that looked at removing inhibitory molecules from the neurons' environment, including some from He's own lab, have found only modest effects on nerve recovery. But now He's team, in collaboration with Mustafa Sahin, MD, PhD, Assistant Professor of Neurology at Children's, demonstrates that re-growth is primarily regulated from within the cells themselves.

"We knew that on completion of development, cells stop growing due to genetic mechanisms that prevent overgrowth," explains He. "We thought that this kind of mechanism might also prevent regeneration after injury."

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## Is Stuttering in Our DNA?

### ***TAU scientists are investigating the genetic factors that underlie stuttering***

Today, three million Americans do, too. Most are able to overcome the handicap, which afflicts 5% of all children - but childhood suffering from stuttering can be traumatic, producing educational, social, and occupational disadvantages.

Intriguing new research from a large-scale international project is providing new insight into the disability. Prof. Ehud Yairi, a long-term Visiting Professor at Tel Aviv University's Sackler School of Medicine, Department of Communication Disorders and founder of the Illinois International Stuttering Research Program at the University of Illinois, is among the leaders of the project.

Prof. Yairi and his fellow researchers are now reporting strong evidence for a significant genetic component to stuttering. They've established that the likelihood of both a spontaneous recovery from stuttering and the development of a chronic disorder are genetically linked.

#### **A Personal Matter**

Prof. Yairi, who suffered from a severe stutter into early adulthood and still exhibits a mild form of the disorder at the age of 69, first suspected that stuttering had genetic ties in his own family. Before him, his grandfather, father, aunts and cousins --on his father's side had exhibited mild to severe forms of stuttering. "I've become an expert in my own problem," he jokes.

"One of the most important goals for us as researchers is to identify ways for making early prognoses, diagnosing both those children who would exhibit chronic stuttering through their lifetimes and those who would recover naturally," says Prof. Yairi. "This will have huge implications for clinical decisions, both for identifying children at high risk for chronic stuttering, as well as selecting the right timing and type of treatment."

#### **An International Affair**

A recent major study supported by NIH took the genetic aspect a step further by genotyping blood samples collected from Israeli, Swedish, and American families with multiple cases of stuttering. This complex study, headed by Professor Nancy Cox, a team member from the University of Chicago School of Medicine, had a branch in Israel, run by Dr. Ruth Ezrati and Professor Minka Hildesheimer, both associates of Tel Aviv University. The researchers were able to identify areas on several chromosomes which indicated a linkage to stuttering, leading the scientists to hope that identification of specific genes underlying stuttering might be isolated.

These findings were published recently in the American Journal of Human Genetics and in the Journal of Communication Disorders.

"The data supports our previous conclusions about the role of genetics in stuttering. Progress in this area will produce some of the most important information in this research in decades," says Prof. Yairi.

#### **Intervene Early, But Don't Panic**

Though stuttering can affect children of all ages, boys are three times more likely to stutter than girls, says Prof. Yairi. He suggests that parents take their children to a speech pathologist within one or two months of the onset of a stutter, though long-term stuttering can be diagnosed only after six to 12 months or so from the stuttering onset.

"All kids exhibit some form of repetition when they are learning to talk, so I would inform parents not to panic if they notice a stutter. Stuttering is a common phenomenon, and most children usually recover," says Prof. Yairi. An early alumnus of Tel Aviv University, he studied at both TAU's Department of Psychology and the Department of Middle Eastern and African Studies despite his own severe stutter. His father, Prof. Yairi notes, had been hoping his son would become an x-ray technician, to avoid having to communicate with people.

#### **Social interactions can alter gene expression in the brain, and vice versa**

Our DNA determines a lot about who we are and how we play with others, but recent studies of social animals (birds and bees, among others) show that the interaction between genes and behavior is more of a two-way street than most of us realize. This is not a new idea to neuroscience, but one that is gaining strength, said University of Illinois entomology and neuroscience professor Gene Robinson, lead author of a review on the subject this week in the journal *Science*. Stanford University biology professor Russell Fernald and Illinois cell and developmental biology and neuroscience professor David Clayton are co-authors.

Genes in the brain are malleable, turning on or off in response to internal and external cues. While genetic variation influences brain function and social behavior, the authors write, social information also alters gene expression in the brain to influence behavior.

Thanks to the newly sequenced genomes of several social animals, including honey bees and zebra finches, and new technologies such as microarrays (which allow researchers to glimpse the activity of thousands of

genes at a time) neuroscientists are gradually coming to understand that "there is a dynamic relationship between genes and behavior," Robinson said. "Behavior is not etched in the DNA."

A critical insight came in 1992, in a study of songbirds led by David Clayton. He and his colleagues found that expression of a specific gene increases in the forebrain of a zebra finch or canary just after it hears a new song from a male of the same species. This gene, *egr1*, codes for a protein that itself regulates the expression of other genes. The finding was not unprecedented; previous studies had shown that genes switch on and off when an animal is trained to perform a task in the laboratory, Robinson said.

But when Clayton's team found this change in gene expression in response to a social signal – a song from a potential competitor, something the bird would likely hear in nature – it drew attention to how powerfully social interactions can alter gene expression in the brain.

"What's more significant to a bird than hearing another bird singing?" Clayton said. "This is going on in the equivalent of our auditory cortex and association cortex, so this is pretty high-level stuff going on in the brain. And this was happening in more or less real time by very naturalistic stimuli."

Reading Clayton's 1992 paper "was a eureka moment for me," Robinson said.

"This just brought it out into the social world, saying that this occurred in animals that have to make a living in the real world and pay attention to a lot of nuanced stimuli," he said. "So I think that was really a very important step in our understanding."

In his own work, Robinson has used microarrays to study this phenomenon on a larger scale and has found that literally thousands of genes turn on or off in the honey bee brain in response to social stimuli. One such gene, called *for* (for foraging), was originally discovered in fruit flies by Marla Sokolowski at the University of Toronto. Flies that carry different versions of *for* show different types of foraging behavior. Each version gives its bearer a behavioral advantage in certain environmental conditions.

Robinson knew that honey bee workers start out working in the hive as nurses and only later graduate to the role of foragers. Perhaps, he reasoned, even though the differences in *for* are etched in the DNA in flies, this same gene in the bee might be more dynamic and help influence the transition from hive work to foraging.

In a study published in 2002, Robinson and his colleagues reported that expression of *for* did in fact increase in the brains of honey bees as they developed into foragers, and manipulating its expression caused bees to forage precociously.

The researchers also found that social factors, in the form of chemical signals called pheromones, induced this "upregulation" of *for*. Foragers produce a pheromone that signals to the younger bees that there are enough foragers. If the foragers are removed from the hive, some young bees develop into foragers much earlier in life than usual.

Sokolowski's work indicated that *for* had changed over evolutionary time, producing two varieties of fruit flies that differed in their behavior. Robinson had found that social information altered expression of the same gene over a much shorter timescale – within the lifespan of a honey bee – also changing its behavior.

"An appreciation of the idea that differences in gene expression can occur over vastly different time scales helps understand some of the complex relationships between genes, brain and behavior," Robinson said.

The picture that is emerging from these and other studies suggests that social signals can have a profound effect on when and how genes function.

An organism's genes, its environment, the social information it receives, "all these things interact," said Clayton. "Experience is constantly coming back in to the level of the DNA and twiddling the dials and the knobs."

### Surprisingly, Female Models Have Negative Effect on Men

#### ***MU study finds unlike women, it is not the same-sex models that affect men***

Story Contact: Jeffrey Beeson, 573-882-9144, BeesonJ@missouri.edu

COLUMBIA, Mo. – Many studies have shown that media images of female models have had a negative impact on how woman view their own bodies, but does this same effect hold true when men view male models? A leading researcher of media effects on body image at the University of Missouri looked at the effect of male magazines on college-age men. Completing three different studies, Jennifer Aubrey, assistant professor of communication in the College of Arts and Science, found that unlike their female classmates, it was not the same-sex models that affected the males negatively, but quite the opposite.

In her research, which will be published in *Human Communication Research*, Aubrey found that the cultural expectation for men is not that they have to be as attractive as their peers, but that they need to be attractive enough to be sexually appealing to women.

In her first study, Aubrey measured male exposure to 'lad' magazines, such as Maxim, FHM and Stuff, which she observes contains two main messages: the visual, which mostly contain sexually suggestive images of women; and textual, which contain articles that speak in a bawdy, male voice about topics including fashion,



sex, technology and pop culture. Aubrey also measured male body self-consciousness (a participant's awareness and tendency to monitor one's appearance) and appearance anxiety (the anticipation of threatening stimuli). Participants were asked questions such as "During the day, I think about how I look," and then asked the same questions a year later.

"We found that reading lad magazines was related to having body self-consciousness a year later," said Aubrey. "This was surprising because if you look at the cover of these magazines, they are mainly images of women. We wondered why magazines that were dominated by sexual images of women were having an effect of men's feelings about their own bodies."

To help answer this question, Aubrey collaborated with University of California-Davis Assistant Professor Laramie Taylor. The researchers divided male study participants into three groups. Group one examined layouts from lad magazines that featured objectified women along with a brief description of their appearances. The second group viewed layouts about male fashion, featuring fit and well-dressed male models. The final group inspected appearance-neutral layouts that featured topics including technology and film trivia.

"Men who viewed the layouts of objectified females reported more body self-consciousness than the other two groups," Aubrey said. "Even more surprising was that the male fashion group reported the least amount of body self-consciousness among the three groups."

Aubrey speculated that the exposure to objectified females increased self-consciousness because men are reminded that in order to be sexually or romantically involved with a woman of similar attractiveness, they need to conform to strict appearance standards.

To test her theory, Aubrey and Taylor completed a third study that involved breaking men into two groups. Group one received lad magazine layouts of sexually idealized females and group two received the same layouts with average-looking 'boyfriends' added to the photos, with captions about how the female models are attracted to the average-looking men.

"We found that the men who view the ads with the average-looking boyfriend in the picture reported less body self-consciousness than the men who saw the ads with just the model," Aubrey said. "When the men felt that the model in the ad liked average-looking guys, it took the pressure off of them and made them less self-conscious about their own bodies."

### **Zoologists: Sea snakes seek out freshwater to slake thirst**

Filed under Environment, Research, Sciences on Thursday, November 6, 2008.

GAINESVILLE, Fla. — Sea snakes may slither in saltwater, but they sip the sweet stuff.

So concludes a University of Florida zoologist in a paper appearing this month in the online edition of the November/December issue of the journal *Physiological and Biochemical Zoology*.

Harvey Lillywhite says it has been the "long-standing dogma" that the roughly 60 species of venomous sea snakes worldwide satisfy their drinking needs by drinking seawater, with internal salt glands filtering and excreting the salt. Experiments with three species of captive sea kraits captured near Taiwan, however, found that the snakes refused to drink saltwater even if thirsty - and then would drink only freshwater or heavily diluted saltwater.

"Our experiments demonstrate they actually dehydrate in sea water, and they'll only drink freshwater, or highly diluted brackish water with small concentrations of saltwater — 10 to 20 percent," Lillywhite said.

Harold Heatwole, a professor of zoology at North Carolina State University and expert on sea snakes, termed Lillywhite's conclusion "a very significant finding."

"This result probably holds the key to understanding the geographic distribution of sea snakes," Heatwole said.

The research may help explain why sea snakes tend to have patchy distributions and are most common in regions with abundant rainfall, Lillywhite said. Because global climate change tends to accentuate droughts in tropical regions, the findings also suggest that at least some species of sea snakes could be threatened now or in the future, he added.

"There may be places where sea snakes are barely getting enough water now," he said. "If the rainfall is reduced just a bit, they'll either die out or have to move."

Sea snakes are members of the elapid family of snakes that also includes cobras, mambas and coral snakes. They are thought to have originated as land-dwelling snakes that later evolved to live in oceans. Most spend all, or nearly all, of their lives in seawater, including giving birth to live young while swimming. A minority, including the kraits that Lillywhite studied, lay eggs and spend at least a small part of their lives on land.



In the lab studies, Lillywhite's team kept snakes caught in the wild near Orchid Island, Taiwan, away from freshwater for two weeks. At the end of that period, dimpling of the snakes' scales indicated they were dehydrated.

The researchers weighed the snakes, freed them in saltwater tanks for up to 20 hours, then weighed them again. None gained appreciably, indicating they didn't drink, despite their thirst. But when the researchers freed the snakes to swim in freshwater tanks, most immediately drank significant amounts. More experiments revealed the snakes would drink only freshwater or highly diluted saltwater.

The kraits may get their freshwater from springs or streams around Orchid Island — deed, the researchers observed far more sea snakes near these freshwater sources than in strictly marine sites, the paper says.

Lillywhite believes the sea snakes that spend their lives in the open ocean drink water from the "lens" of freshwater that sits atop saltwater during and after rainfall, before the two have had a chance to mix. That would explain why some seawater lagoons, where the waters are calmer due to protection from reefs, are home to dense populations of sea snakes - the freshwater lens persists for longer periods before mixing into saltwater.

Rather than helping sea snakes gain water, the snakes' salt gland may help the snakes with ion balance - moving excess salts from the bloodstream, Lillywhite said.

Some sea snake species living in dry regions may already be suffering as a result of climate change. Lillywhite said a colleague in Australia, which is in the midst of a historic drought, has observed declines and possible extinctions in some species at Ashmore Reef, home to the most diverse and abundant population of sea snakes in the world.

"We are trying to look at rainfall in that region and see if there is a correlation," Lillywhite said.

He added that his findings also raise questions about the accepted wisdom that other marine reptiles, including sea turtles, satisfy their freshwater needs by drinking saltwater.

### **Dry spells spelled trouble in ancient China** ***Weakening of summer monsoons to blame***

Chinese history is replete with the rise and fall of dynasties, but researchers now have identified a natural phenomenon that may have been the last straw for some of them: a weakening of the summer Asian Monsoons.

Such weakening accompanied the fall of three dynasties and now could be lessening precipitation in northern China. Results of the study, led by researchers from the University of Minnesota and Lanzhou University in China, appear in this week's issue of the journal *Science*.

The work rests on climate records preserved in the layers of stone in a 118-millimeter-long stalagmite found in Wanxiang Cave in Gansu Province, China. By measuring amounts of the elements uranium and thorium throughout the stalagmite, the researchers could tell the date each layer was formed. And by analyzing the "signatures" of two forms of oxygen in the stalagmite, they could match amounts of rainfall--a measure of summer monsoon strength--to those dates. The stalagmite was formed over 1,810 years; stone at its base dates from A.D. 190, and stone at its tip was laid down in A.D. 2003, the year the stalagmite was collected.

"It was unexpected that a record of surface weather would be preserved in underground cave deposits," said David Verardo, director of the National Science Foundation (NSF)'s Paleoclimatology Program, which funded the research. "These results illustrate the promise of paleoclimate science to look beyond the obvious and see new possibilities."

"Summer monsoon winds originate in the Indian Ocean and sweep into China," said Hai Cheng, author of the paper and a scientist at the University of Minnesota. "When the summer monsoon is stronger, it pushes farther northwest into China."

These moisture-laden winds bring rain necessary for cultivating rice. But when the monsoon is weak, the rains stall farther south and east, depriving northern and western parts of China of summer rains.

A lack of rainfall could have contributed to social upheaval and the fall of dynasties.

The researchers discovered that periods of weak summer monsoons coincided with the last years of the Tang, Yuan and Ming dynasties, which are known to have been times of popular unrest. Conversely, the scientists found that a strong summer monsoon prevailed during one of China's "golden ages," the Northern Song Dynasty.

The ample summer monsoon rains may have contributed to the rapid expansion of rice cultivation from southern China to the midsection of the country. During the Northern Song Dynasty, rice first became China's main staple crop, and China's population doubled. "The waxing and waning of summer monsoon rains are just one piece of the puzzle of changing climate and culture around the world," said Larry Edwards, geologist at the University of Minnesota and a co-author of the paper.

For example, the study showed that the dry period at the end of the Tang Dynasty coincided with a previously identified drought halfway around the world, in Meso-America, which has been linked to the fall of the Mayan civilization. The study also showed that the ample summer rains of the Northern Song Dynasty coincided with the beginning of the well-known Medieval Warm Period in Europe and Greenland.

During this time--the late 10th century--Vikings colonized southern Greenland. Centuries later, a series of weak monsoons prevailed as Europe and Greenland shivered through what geologists call the Little Ice Age.

In the 14th and early 15th centuries, as the cold of the Little Ice Age settled into Greenland, the Vikings disappeared from there. At the same time, on the other side of the world, the weak monsoons of the 14th century coincided with the end of the Yuan Dynasty.

A second major finding concerns the relationship between temperature and the strength of the monsoons. For most of the last 1,810 years, as average temperatures rose, so, too, did the strength of the summer monsoon.

That relationship flipped, however, around 1960, a sign that the late 20th century weakening of the monsoon and drying in northwestern China was caused by human activity.

If carbon dioxide is the culprit, as some have proposed, the drying trend may well continue in Inner Mongolia, northern China and neighboring areas on the fringes of the monsoon's reach.

If, however, the culprit is man-made soot, as others have proposed, the trend could be reversed, the researchers said, by reduction of soot emissions.

*The research also was supported by the National Science Foundation of China and the Gary Comer Science and Education Foundation.*

### **UC Davis researchers discover Achilles' heel in pancreatic cancer** ***Starving cancer cells of arginine cuts proliferation in half***

UC Davis Cancer Center researchers have discovered a metabolic deficiency in pancreatic cancer cells that can be used to slow the progress of the deadliest of all cancers.

Published in the October issue of the *International Journal of Cancer*, study results indicate that pancreatic cancer cells cannot produce the amino acid arginine, which plays an essential role in cell division, immune function and hormone regulation. By depleting arginine levels in cell cultures and animal models, the team was able to significantly reduce pancreatic cancer-cell proliferation.

"There have been few significant advances in 15 years of testing available chemotherapy to treat pancreatic cancer," said Richard Bold, chief of surgical oncology at UC Davis and senior author of the study. "The lack of progress is particularly frustrating because most patients are diagnosed after the disease has spread to other organs, eliminating surgery as an option. We have to turn back to basic science to come up with new treatments."

Bold explained that average survival time for those diagnosed with pancreatic cancer is just four-and-a-half months, although chemotherapy can extend that prognosis up to six months. "There is a dire need to find new options for these patients. While our findings do not suggest a cure for pancreatic cancer, they do promise a possible way to extend the life expectancies of those diagnosed with it," Bold said.

Bold and his colleagues hypothesized that pancreatic cancer cells lack the ability to produce arginine. In human pancreatic tumors, they measured levels of an enzyme — argininosuccinate synthetase — required to synthesize arginine. The enzyme was not detected in 87 percent of the 47 tumor specimens examined, suggesting that the majority of pancreatic cancers require arginine for cell growth because of an inability to synthesize the amino acid.

The researchers then conducted further tests using pancreatic cell lines that represent the varying levels of argininosuccinate synthetase observed in human tumor specimens. Focusing on the lines with lowest levels, the researchers depleted arginine levels in cultures of pancreatic cell lines using arginine deiminase, an enzyme isolated from a *Mycoplasma* bacteria.

The enzyme was modified by adding polyethylene glycol chains to increase size and circulatory time.

The researchers found that exposing the pancreatic cancer cell lines to the modified arginine deiminase enzyme inhibited cancer-cell proliferation by 50 percent. They then treated mice bearing pancreatic tumors with the same compound and found an identical outcome: a 50 percent reduction in tumor growth. According to Bold, the current study represents a unique approach to cancer treatment in that it is one of the first to identify a metabolic pathway that can be leveraged to interrupt cancer growth.

"Instead of killing cells as with typical chemotherapy, we instead removed one of the key building blocks that cancer cells need to function," Bold said.

Metabolic interruptions like this one are also being studied for their potential in treating cancers of the blood, such as leukemia and lymphoma. In those cases, depleting the amino acid asparagine may be used in slowing cancer-cell growth.

Bold and his colleagues are continuing their laboratory work on the effects of arginine deprivation on pancreatic cancer. They will next be looking for ways to increase pancreatic cell sensitivity to arginine deprivation. The researchers have also begun designing human clinical trials in cooperation with the manufacturer of arginine deiminase, Polaris Pharmaceuticals.

"We're looking at whether we can combine this treatment with certain kinds of chemotherapy," Bold said. "This additional research is needed to inform the clinical work and move it forward more quickly. The better we understand this process, the more we can use it in the fight against pancreatic cancer."

*Additional study authors included Tawnya Bowles, Joseph Galante, Colin Parsons and Subbulakshmi Virudachalam of the UC Davis Department of Surgery; and Randie Kim and Hsing-Jien Kung of the UC Davis Department of Biochemistry and Molecular Medicine. The study was funded by DesignRxPharmacologics of Vacaville, Calif.*

## **Tolerance Over Race Can Spread, Studies Find**

**By BENEDICT CAREY**

This was supposed to be the election when hidden racism would rear its head. There was much talk of a "Bradley effect," in which white voters would say one thing to pollsters and do another in the privacy of the booth; of a backlash in which the working-class whites whom Senator Barack Obama had labeled "bitter" would take their bitterness out on him.

But lost in all that anguished commentary, experts say, was an important recent finding from the study of prejudice: that mutual trust between members of different races can catch on just as quickly, and spread just as fast, as suspicion.

In some new studies, psychologists have been able to establish a close relationship between diverse pairs — black and white, Latino and Asian, black and Latino — in a matter of hours. That relationship immediately reduces conscious and unconscious bias in both people, and also significantly reduces prejudice toward the other group in each individual's close friends.

This extended-contact effect, as it is called, travels like a benign virus through an entire peer group, counteracting subtle or not so subtle mistrust.

"It's important to remember that implicit biases are out there, absolutely; but I think that that's only half the story," said Linda R. Tropp, an associate professor of psychology at the University of Massachusetts. "With broader changes in the society at large, people can also become more willing to reach across racial boundaries, and that goes for both minorities and whites."

Mr. Obama's election notwithstanding, institutional and individual prejudice still infects many areas of modern life, all experts agree. And this year, worries about the economy may have trumped any persistent concerns about race.

Yet to the extent that race played a role at all, it seemed to break more in Mr. Obama's favor than against him. In voter surveys, most of the 17 percent of white voters who said race played some part in their decision pulled the lever for Mr. McCain; but among all voters who took race into account, Mr. Obama won the majority.

"I'm a Republican, and for me to vote for Obama I had to have a certain level of trust, that he was going to do the right thing, that he wasn't going to be small-minded, that he wasn't going to take care of one group of people over another," said Nelson Montgomery, 50, a white sales executive in Buffalo who lived in a black neighborhood in Houston early in his career.

"What it came down to," Mr. Montgomery said, "is that we're so polarized right now, we're only hearing from the fringe on either side, and we need more than anything to build trust. And I felt he could do that."

In studies over the past few years, researchers have demonstrated how quickly trust can build in the right circumstances. To build a close relationship from scratch, psychologists have two strangers come together in four hourlong sessions. In the first, the two share their answers to a list of questions, from the innocuous "Would you like to be famous? In what way?" to the more serious, like "If you could change anything about the way you were raised, what would it be?"

In the second session, the pair competes against other pairs in a variety of timed parlor games. In the third, they talk about a variety of things, including why they are proud to be a member of their ethnic group, whether Latino, Asian, white or black. Finally, they take turns wearing a blindfold, while their partner gives instructions for navigating a maze.

Trivial as they may sound, those exercises create a relationship "that is as close as any relationship the person has," said Art Aron, a social psychologist at Stony Brook University who developed the program with his wife, Elaine N. Aron.

The new relationship can last months or longer, and it almost immediately lowers a person's score on a variety of prejudice measures. Moreover, it significantly reduces anxiety during encounters with other members of that second group, as gauged by stress hormone levels in the saliva.

In a series of studies, Art Aron and others have found that, by generating a single cross-group friendship, they can quickly improve relations between cliques that have been pitted against one another in hostile competitions. In a continuing study of some 1,000 new students at Stony Brook, Dr. Aron has found that merely being in the same class where other interracial pairs were interacting can reduce levels of prejudice.

The reason such changes emerge, some psychologists argue, is that people have a selfish urge to expand their own identities through others — to make themselves a part of others' lives, and vice versa, as lovers, parents, colleagues, friends. Studies find that that is exactly what happens in a relationship: people are not merely aware of their closest friends' problems but to some extent feel the sting, the humiliation, the injustice.

Psychologists can manipulate this need for self-expansion. In one recent experiment, led by Stephen Wright, a psychologist at Simon Fraser University in British Columbia, researchers had 47 students describe their workloads and activities and made each student feel either overextended or in a rut, based on bogus personality tests.

"It's easy enough to do, because students always feel both overwhelmed and in a rut," Dr. Wright said. Those led to feel in a rut, he went on, "were more interested than the others in having a friendship with someone with a name that is clearly from a minority group."

This impulse pushes against any implicit or subconscious bias a person may have. When larger issues are in play, race can shrink quickly in importance. In the late 1960s, when the black politician Richard G. Hatcher was vying to become mayor of Gary, Ind., one neighborhood near the steel mills was running nearly 90 percent against him, said Thomas Pettigrew, a research professor in social psychology at the University of California, Santa Cruz, who helped do the polling. It turned out that many people there were most concerned about a nearby city dump that cast a bad smell over the neighborhood.

After he was elected, Mayor Hatcher closed the dump, and the next election he got nearly 40 percent of the vote from the neighborhood.

"A lot of people living there cared a lot more about the dump than the color of their mayor," Dr. Pettigrew said. About Mr. Obama's election, he added, "the economic crisis I think has had the same impact."

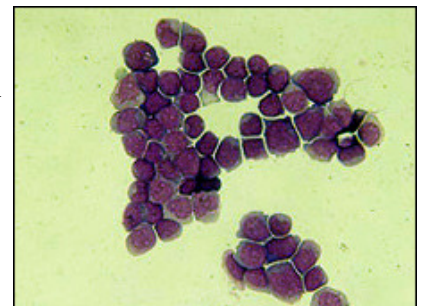
### **Cancer genetic blueprint revealed**

#### ***Scientists have decoded the complete DNA of a cancer patient and traced her disease to its genetic roots.***

The Washington University team identified 10 gene mutations which appeared key to the development of the woman's acute myeloid leukaemia. Just two of these had been linked to the disease before.

The sequencing technique, described in the journal *Nature*, could be applied to other cancers and aid the design of targeted drugs.

The researchers took two samples from the woman in her 50s - who later died from the disease - and examined the DNA for differences. One sample was taken from healthy skin cells, the other from bone marrow tissue made up of cancerous cells. They found that virtually every cell in the tumour sample had nine of the key mutations.



#### ***Leukaemia targets cells in bone marrow which form blood***

Like most cancers, acute myeloid leukaemia (AML) - a cancer of blood-forming cells in the bone marrow - arises from mutations that accumulate in people's DNA over the course of their lives.

However, little is known about the precise nature of those changes and how they disrupt biological pathways to cause the uncontrolled cell growth that is the hallmark of cancer.

Previous efforts to decode individual human genomes have looked at common points of DNA variation that may be relevant for disease risk. In contrast the Washington team, using a gene sequencing technique, were able to sift through the three billion pairs of chemical bases that make up the human genome to pull out the mutations that contributed to the patient's cancer.

#### **True landmark**

Geneticist Dr Francis Collins, a former director of the US National Human Genome Research Institute, called the study a "true landmark in cancer research".

He said: "In the past, cancer researchers have been 'looking under the lamp-post' to find the causes of malignancy - but now the team from Washington University has lit up the whole street. "This achievement ushers in a new era of comprehensive understanding of the fundamental nature of cancer, and offers great promise for the development of powerful new approaches to diagnosis, prevention and treatment."

Three of the newly-discovered mutations were in genes that normally suppress tumour growth, and four were in genes linked to the spread of cancer.

The other appears to affect the transport of drugs into the cells, possibly fuelling resistance to cancer therapy.

The researchers are still looking for other gene mutations which may also play a part. They also examined tumour samples from another 187 AML patients, but found none had any of the eight new mutations.

Lead researcher Dr Richard Wilson said: "This suggests that there is a tremendous amount of genetic diversity in cancer, even in this one disease. "There are probably many, many ways to mutate a small number of genes to get the same result, and we're only looking at the tip of the iceberg in terms of identifying the combinations of genetic mutations that can lead to AML." The researchers suspect that the mutations occurred one after another, with each pushing the cell closer to malignancy.

Kat Arney, of the charity Cancer Research UK, said: "This is a very important piece of research, not only for our understanding of leukaemia but for many other types of cancer. "Thanks to advances in technology it is now possible to unlock the genetic secrets within cancer cells, which will be the key to better diagnostic tools and treatments in the future."

Ken Campbell, of Leukaemia Research said: "Although it is very early days, it is realistic to think that these findings could lead to new treatments. "Its wider application to other cancers may be limited though - the technique is particularly valuable for blood cancers in which the chromosome changes are usually simpler than in solid tumours at the time of diagnosis."

### **Why hair bleach is a murderer's best friend**

\* 06 November 2008

\* NewScientist.com news service

\* **Jeff Hecht**

BUDDING crime-scene investigators take note: a common household bleach can render the forensic techniques for detecting blood useless.

There are two types of bleach found in household cleaning products. Chlorine-based bleaches are known to make bloodstains invisible, but applying chemicals such as luminol or phenolphthalein will still reveal the presence of haemoglobin - crucial for identifying blood - even after up to 10 washes. In contrast, oxygen bleach, which contains an oxidising agent such as hydrogen peroxide, erases all trace of haemoglobin. Its effect seems to have been untested until now.

Fernando Verdú and his team at the University of Valencia, Spain, soaked bloodstained fabric in oxygen bleach for 2 hours and compared the results with unwashed controls. They found that the stains faded after bleaching but remained visible. However, luminol, phenolphthalein and direct haemoglobin tests failed to find any haemoglobin in them (Naturwissenschaften, DOI: 10.1007/s00114-008-0466-9). The mechanism by which the hydrogen peroxide alters haemoglobin is unclear.

Chlorine bleach can itself produce false positives on luminol tests, but there are ways to counteract this. Also a false positive can be corrected by further testing. Oxygen bleach creates a much greater problem: "A stain being visible but unreactive could be passed over as viable evidence," says Jonathan Creamer of Vanderbilt University in Nashville, Tennessee. Forensic scientists will only test for DNA, for example, if they first identify a human sample. If the chemical tests show no blood, "you're definitely missing the chance for more information," says Creamer.

"Loss of any evidence can have an effect on an investigation," says Gillian Leak, a specialist in blood pattern analysis at the UK Forensic Science Service. All is not lost, though. Leak says that although washing can hide or remove some blood, "we can still get results from stains embedded within seams."

### **Plastic not so fantastic for lab experiments**

\* 19:00 06 November 2008 \* NewScientist.com news service

\* **Ewen Callaway**

Worries over a chemical that may seep out of some plastics has caused many consumers to abandon reusable water bottles. Now scientists might want to do the same thing with their test tubes.

It seems ingredients in commercial plastic test tubes used by labs around the world can block some biological reactions, potentially leading researchers to bogus conclusions about whether drugs work or not.

Water alone is enough to leach these chemicals out of plastic tubes, says Andrew Holt, a biochemist at the University of Alberta, whose team noticed the effect while testing experimental drugs that could potentially treat Parkinson's disease.

The finding backs up anecdotal evidence from scores of scientists that plastics seem to affect some experiments, Holt says. "People are clearly aware that plastics can cause problems. Quite remarkably, nobody appears to have done what we were forced to do," he says.

## Extra ingredients

After noticing that his lab's measurements of an enzyme called MAO-B were all over the chart, Holt and his colleagues set out to identify the cause. The likeliest culprits were plastic microcentrifuge tubes – the molecular biologist's equivalent to a mixing bowl.

Water stored in the tubes from several manufacturers was found to block the MAO-B enzyme by as much as 40%, Holt's team found. When they analysed the contents of the water they found traces of an antimicrobial compound and a chemical that prevents water from sticking to the plastic – both added intentionally to the plastic by the manufacturers.

Furthermore, plastic pipette tips – a one-use product that delivers small amounts of liquid for experiments – also leached chemicals that block biological reactions. And chemicals from plastic plates used in protein experiments actually made the MAO-B enzyme more active.

These effects could distort experiments enough to make a big difference in research. "I think it's inevitable that a lot of data that's in the public domain will be skewed in some way," Holt says, though he hasn't yet identified papers with erroneous data or conclusions. "The end result is that researchers are wasting massive amounts of time and massive amounts of money," he adds.

The problem may even extend to sterile plastic containers that researchers use to grow cells, says Simonetta Sipione, who is also at the University of Alberta, though was not involved in the study. Sipione studies Huntington's disease and suspects that leaching from plastics might have caused the mysterious death of cultured brain cells in her lab.

## Washing the dishes

When Holt first suspected that plastics were causing problems for his lab, he contacted the manufacturer of his pipette tips, a German company called Sarstedt, who could not replicate his lab's data.

Holt says that is because they didn't perform the experiment as sensitively as his team. "I never heard back from them, and that was more than a year ago," he says.

However, Holt doesn't hold companies like Sarstedt responsible. Manufacturers add antimicrobial and static-reducing chemicals to make lab-ware more useful for scientists, and it seems that few if any researchers have alerted companies to problems with their plastics, he says.

For now, Holt's lab washes suspected plastic immediately before experiments to leach out as many chemicals as possible. But the time-consuming procedure is untenable as a permanent solution, he says.

Leached chemicals seem to block some proteins, but not others. Holt hopes manufacturers see an opportunity and create plastic wear with a variety of additives, so researchers can pick the one that's least likely to mess with their experiments. "It leaves us in a mess, but I don't think it's a mess that we can't address," he says. *Journal reference: Science (DOI: 10.1126/science.1162395)*

## Montana State University researchers find gene that regulates mold's resistance to drugs

BOZEMAN, Mont. -- Montana State University scientists concerned about lethal mold infections have found a gene that regulates the mold's resistance to drugs.

The gene, called *srbA*, allows molds to thrive during infections even when inflammation reduces its oxygen supply, said Robert Cramer, senior author of a paper published in the Nov. 7 issue of *PLoS Pathogens*. When the gene is removed, the mold becomes much more vulnerable to lack of oxygen and can no longer grow to cause disease.

The gene is found in humans and molds, but the researchers studied it in a common mold called *Aspergillus fumigatus*, said Cramer, assistant professor of fungal pathogenesis in MSU's Department of Veterinary Molecular Biology. *A. fumigatus* can invade the lungs and cause dangerous diseases, including Invasive Pulmonary Aspergillosis. Patients with a compromised immune system, especially organ transplant patients, are particularly at risk.

"The incidence of potentially lethal infections caused by normally benign molds has increased tremendously over the last two decades," the researchers wrote.

The scientists discovered the value of *srbA* after creating a mutant version of the fungus without the gene, Cramer said. Tests showed that the loss of *srbA* affected 87 genes in the fungus. Without the gene, the mutant could no longer grow when oxygen was limited, which occurs during mold infections. The mutant mold without *srbA* could no longer cause disease. It was also highly susceptible to antifungal drugs, more vulnerable than the original, complete mold.

Further study showed that *srbA* plays a critical role in the making of ergosterol, the fungal-form of cholesterol, Cramer said. The gene in humans is associated with the making of cholesterol. Ergosterol and cholesterol are necessary components of cell membranes.

"The reason we're interested is because ergosterol is a target for most of the antifungal drugs that are available," Cramer said. "These drugs target the synthesis of ergosterol. ... If you get rid of ergosterol, you kill the mold."

Sven Willger, a postdoctoral researcher in Cramer's lab and first author of the PLoS Pathogens paper, said the absence of *srbA* changed the way the mold cells grew. Instead of growing from the tip, they branched off from several other locations. The confusion became apparent under a transmission electron microscope.

The researchers said in their paper that they demonstrated for the first time that it is significant that invasive molds adapt to reduced oxygen levels during infection.

*Besides Cramer and Willger, MSU co-authors of the paper are Srisombat Puttikamonkul and Nora Grahl, both graduate students in Cramer's lab; and James Burritt, assistant professor of microbiology. Co-authors from other institutions are Kwang-Hyung Kim and Christopher Lawrence from the Virginia Bioinformatics Institute, and Laurel Metzler, Robert Barbuch and Martin Bard from Indiana University-Purdue University.*

### **Overnight Hemodialysis Dramatically Improves Survival**

**Philadelphia, PA (October 30, 2008)** — For hemodialysis patients, undergoing dialysis for eight hours overnight, three times weekly, reduces the risk of death by nearly 80 percent, compared to conventional, four-hour dialysis, according to research being presented at the American Society of Nephrology's 41st Annual Meeting and Scientific Exposition in Philadelphia, Pennsylvania.

In a study led by Ercan Ok, MD, of Ege University in Izmir, Turkey, 224 dialysis patients were switched to overnight dialysis. The patients spent three nights a week at the dialysis center where they underwent eight hours of continuous hemodialysis. The patients adjusted well to overnight hemodialysis. "After an adaptation period of a month, all patients slept during the night without any complaint," says Dr. Ok.

The patients remained on overnight hemodialysis for about one year. Their outcomes were compared with those of a similar group of patients who continued on conventional dialysis: four hours, three days per week.

Overnight dialysis led to improvements in a wide range of outcomes. "The hospitalization rate during follow-up was one-fourth of that observed in patients treated with four-hour conventional hemodialysis," comments Dr. Ok. "Most importantly, our results confirmed that longer dialysis produces significantly better patient outcomes, with a 78 percent reduction in mortality rate." Patients receiving overnight hemodialysis had better blood pressure control, leading to a two-thirds reduction in blood pressure medications. They were also at lower risk of blood pressure drops during dialysis, a common problem with conventional hemodialysis. Levels of the mineral phosphate decreased toward normal, despite a 72 percent reduction in medications used to lessen phosphate absorption.

The need for other medications decreased as well. All of these outcomes either did not change or deteriorated in patients on four-hour conventional dialysis.

Most patients in the overnight hemodialysis group mentioned an increase in appetite. They gained weight, and their serum protein (albumin) levels increased. Many patients were able to return to work, reporting improved job performance and better mental (cognitive) functioning.

More frequent and/or longer dialysis regimens are a promising alternative to addressing the "unacceptably high" risk of death among dialysis patients, according to Dr. Ok. Although home dialysis is may be the best approach (aside from kidney transplantation), it is not an option for most patients.

Previous studies of overnight, thrice-weekly hemodialysis have shown impressive results, with ten-year survival rates as high as 75 percent. The new trial is the first prospective, controlled study to compare the results of eight-hour versus four-hour hemodialysis, performed in the dialysis center.

The study has some important limitations, including the fact that patients were not randomly assigned to the two dialysis strategies. With an average age of 45, the patients were younger than the general population of dialysis patients—few older patients were willing to switch to overnight hemodialysis. In addition, the followup period was relatively short.

However, given the clear superiority of eight-hour dialysis, the researchers do not think the results would be changed with long-term observation. Dr. Ok adds, "We expect that these data would be convincing to the whole of society—including physicians, patients, health authorities, and social security institutions—for the necessity of longer hemodialysis in order to improve high mortality and morbidity."

The study was supported by a grant from the European Nephrology Dialysis Institution. The study was conducted in Fresenius Medical Care (FMC) Turkey clinics. Ercan Ok, MD and Ali Basci, MD are members of the Scientific Advisory Board of FMC Turkey; Siddig Momin Adam, MD, is a nephrologist in a FMC Turkey Clinic.

The study abstract, "Eight-Hour Nocturnal In-Center Hemodialysis Provides Survival Benefit Over Four-Hour Conventional Hemodialysis," (F-FC317) will be presented as part of a Free Communications session on the topic of "Outcomes Associated with Dialysis Mortality and Delivery" on Friday, November 7 at 5:24 p.m. in Room 204 B/C of the Pennsylvania Convention Center in Philadelphia, PA.



## **General anesthesia for hernia surgery in children and risk of later developmental problems**

Children under the age of three who had hernia surgery showed almost twice the risk of behavioral or developmental problems later compared to children who had not undergone the surgery, according to a study by researchers at Columbia University Mailman School of Public Health and the College of Physicians and Surgeons. The study included 383 children who were born into the New York State Medicaid system between 1999 and 2001 who had surgery performed under general anesthesia to repair a groin hernia.

The researchers compared this group of children to 5,050 randomly selected, age-matched children in the Medicaid system, and found that five percent of the children exposed to anesthesia and 1.5 percent of the children in the control group were eventually diagnosed with a developmental or behavioral disorder. After adjusting for age, gender, race and such complicating birth diagnoses as low weight, the association between hernia surgery under general anesthesia and behavioral diagnoses was twice that in children who did not have surgery.

"We suspect that children who had hernia surgery and its associated exposure to general anesthesia during these operations might have played a role in the jump in risk," according to Charles DiMaggio, PhD, assistant professor of clinical Epidemiology at the Mailman School of Public Health, and lead author. "While there is no hard evidence that there is any causal association between anesthesia and developmental outcomes in children, research in animal models indicates that there may be some association between the types of anesthesia commonly used and neuronal or brain cell-level injury," said Dr. DiMaggio. "The early concern is, could these data be extrapolated to humans?"

According to Dr. DiMaggio, while the current study found an association between anesthesia use and neurodevelopmental problems, these are still preliminary findings, and not a reason to keep children from needed surgery. "This underscores the urgent need for more rigorous clinical research on the long-term effects of surgery and anesthesia in children," says Dr. DiMaggio.

*The findings were presented at the American Society of Anesthesiologists annual meeting held in Orlando, Florida on October 18-22.*

## **Paleontologists doubt 'dinosaur dance floor' *Potholes or tracks? Both sides team for follow-up study***

SALT LAKE CITY – A group of paleontologists visited the northern Arizona wilderness site nicknamed a "dinosaur dance floor" and concluded there were no dinosaur tracks there, only a dense collection of unusual potholes eroded in the sandstone.

So the scientist who leads the University of Utah's geology department says she will team up with the skeptics for a follow-up study.

"Science is an evolving process where we seek the truth," says Marjorie Chan, professor and chair of geology and geophysics, and co-author of a recent study that concluded the pockmarked, three-quarter-acre site in Vermilion Cliffs National Monument was a 190-million-year-old dinosaur "trample surface".

"We went through the proper scientific process of careful study, comparisons with other published works and peer review" of the study by independent scientists, Chan adds. "We gave the project considerable critical thought and came up with a different interpretation than the paleontologists, but we are open to dialogue and look forward to collaborating to resolve the controversy."

On Oct. 30 – more than a week after the Utah study was publicized worldwide – four scientists hiked to the remote wilderness-area site: paleontologist Brent Breithaupt, director and curator of the University of Wyoming's Geological Museum; U.S. Bureau of Land Management paleontologist Alan Titus and geologist Rody Cox; and paleontologist Andrew Milner of the St. George (Utah) Dinosaur Discovery Site at Johnson Farm.

They saw dinosaur tracks en route, but none in the pockmarked "dance floor."

"There simply are no tracks or real track-like features at this site," Breithaupt says. "We will be investigating the formation of these features in the upcoming study. Science works best when scientists work together."

Chan and Winston Seiler, who conducted the research as part of his master's thesis, say they are not retracting their study, which was published in the October issue of *Palaios*, an international paleontology journal. But they acknowledge there are strong arguments for the features being potholes rather than dinosaur tracks. The original study cited the possibility that the features were potholes and outlined arguments against it.

Chan says if the features are potholes, they are extremely unusual compared with typical potholes on the Colorado Plateau – and their formation still needs to be explained fully. She will work with Breithaupt and the others to examine the site in greater detail.

"A reinterpretation could emerge, but those conclusions have not yet been written as a scientific paper and need to be submitted to a journal for publication after peer review by other scientists," she says.

Nevertheless, the University of Utah geologists feel obligated to inform the public of the difference of opinion because of wide publicity about the "dinosaur dance floor."

"The public interest has been tremendous, and fortunately there are many other fantastic, accessible, documented dinosaur track sites than can be visited in the area," Breithaupt says.

Seiler spent considerable time at the unusual site. He acknowledges that the dinosaur track interpretation is controversial, further study is warranted, and if the paleontologists turn out to be correct, "that's part of science."

Chan adds: "This is how science works, and we'll have to see how it shakes out in the end."

### **China tells rich states to change**

Chinese Premier Wen Jiabao has said developed countries should change their "unsustainable lifestyles" to tackle global warming.

Mr Wen said richer nations should help poorer ones solve the global problem.

United Nations climate chief Yvo de Boer said rich countries had to transfer cleaner energy technologies to developing nations.

The two were speaking at a two-day conference in Beijing discussing climate change.

Mr Wen said the international community must not waver in its determination to tackle climate change.

But he made it clear where the main responsibility lay.

Developed countries had a "responsibility to tackle climate change and should alter their unsustainable lifestyle", he said.

### **'Weightier problem for us'**

Among others, Chinese officials have previously suggested that rich nations use 1% of their gross domestic product to pay for the transfer of clean energy technologies to developing nations.

While promising China will play its part, Mr Wen said his country faced a more difficult task than developed countries.

He said it took rich countries several decades to get round to saving energy and cutting greenhouse gas emissions, which cause global warming.

"China has to solve the same problem in a relatively much shorter period," he said.

China has so far declined to place a cap its greenhouse emissions.

### **Technology transfer**

Mr de Boer, executive secretary of the UN Framework Convention on Climate Change, also said richer nations should pay more to tackle the problem.

"If international technology transfer happens, countries like China will be able to take action which is not affordable to them at the moment," he said, speaking at the same conference as the Chinese premier.

He urged developed countries to speed up the transfer of these technologies.

The current treaty that tries to limit greenhouse gas emissions - the Kyoto Protocol - runs out in 2012.

Negotiators will start discussing what will replace it in Poland next month.