

## Back to normal: Surgery improves outcomes for spine patients

ROSEMONT, Ill.— People with the spine disease called degenerative spondylolisthesis\* -- who choose surgical treatment -- experience substantially greater relief from pain over time compared to those who do not have surgery, according to a study published in the June 2009 issue of The Journal of Bone and Joint Surgery (JBJS). In the past, physicians had been uncertain whether surgery provided significantly greater relief for patients, but these results help to confirm the advantages to surgery.

"There are thousands of surgeries completed each year to address degenerative spine conditions, yet, there has never been a large-scale trial to give us evidence that the surgeries really work, as compared to non-operative approaches," said study author James Weinstein, DO, MS, Third Century Professor and Chair of the departments of orthopaedics at Dartmouth Medical School and Dartmouth-Hitchcock Medical Center.

Dr. Weinstein and his colleagues collected data from 607 men and women diagnosed with spondylolisthesis who were enrolled in the Spine Patient Outcomes Research Trial (SPORT), a multi-center study that included participants from 13 medical centers in 11 states. The study was the largest ever conducted of spondylolisthesis patients.

"Until this study, our 'evidence' was anecdotal and based on patient reports. We wanted data-based, scientific evidence that we could share with patients to help them make their decisions about taking an operative vs. non-operative approach," Weinstein said.

Prior to completion of the study, SPORT looked at the three most common back conditions leading to surgery, which are:

- \* herniated disc;
- \* spinal stenosis; and
- \* spinal stenosis with degenerative spondylolisthesis.

To be included in the study, all patients had to meet certain criteria, including:

- \* nerve pain in the legs
- \* spinal stenosis revealed on cross-sectional imaging
- \* degenerative spondylolisthesis evident in radiograph imaging
- \* symptoms which lasted for at least 12 weeks
- \* physician confirmation that the patient was a surgical candidate.

"Our results indicate that in these patients, there was a clear advantage for surgery," said Dr. Weinstein. "Patients felt relief faster and at two and four years, reported better function, less pain, and higher satisfaction than those who chose to go the non-surgical route."

Approximately 80 percent of Americans suffer from back pain at some point in their lives. Back pain is the most common cause of work-related disability, as well as the most expensive in terms of workers compensation and medical costs. Degenerative spondylolisthesis is one example of this kind of painful back condition.

"Degenerative spine disease can be a debilitating condition. When well informed, surgery is a good treatment choice," said Weinstein.

SPORT investigators will be releasing additional studies focusing on cost-effectiveness and other factors in coming months.

**\* Degenerative spondylolisthesis occurs when laxness in the spine causes one vertebra to slide forward and press against nerves, causing pain in the back and legs. The condition often occurs as a result of the aging process.**

**More Information:** SPORT is the first comprehensive study to look at different ways of treating low back and leg pain and how effective they are for patients. The trial was funded by the National Institutes of Health (NIH) in recognition of how prevalent back problems are, and how disabling they can be. The research is meant to give patients and their physicians solid information to help guide them as they make decisions about how to treat their conditions. Approximately 2500 patients took part in the 5-year study.

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## **Cancer patients want genetic testing to predict metastasis risk** ***UCLA study shows results have little effect on mood, quality of life***

If you had cancer and a genetic test could predict the risk of the tumor spreading aggressively, would you want to know – even if no treatments existed to help you?

An overwhelming majority of eye cancer patients would answer yes, according to a new UCLA study published in the June edition of the *Journal of Genetic Counseling*.

"Our goal was to explore what people with cancer want," explained Dr. Tara McCannel, director of the Ophthalmic Oncology Center at UCLA's Jules Stein Eye Institute and a Jonsson Comprehensive Cancer Center researcher. "We learned that patients want to know their prognosis, good or bad, even when there are no treatments at present for their condition."

The UCLA study surveyed 99 patients who had been diagnosed with ocular melanoma, which develops in the pigmented layers under the retina. Half of the patients had undergone localized radiation to shrink the tumor. The rest of the group also underwent radiation, but first had cells biopsied from their tumors. These cells were grown in culture and studied for a missing copy of chromosome 3 —the genetic marker most strongly linked to rapid metastatic disease.

Patients whose tumors contain the genetic marker have at least a 50 percent chance of death within five years, due to swift spreading of the tumor to the liver and other organs. Aggressive cases can result in blindness and death in as quickly as a year.

In the UCLA study, all patients were asked to evaluate their interest in receiving genetic testing results related to prognosis. A whopping 98 patients responded that they would have wanted predictive testing at the time of their treatment. Only one patient declined.

Additionally, 98 percent of the respondents stated that supportive counseling should be offered when patients receive their test results.

"We were surprised to see such a unanimous response," admitted McCannel. "We expected some patients would prefer not to know, but the numbers consistently said otherwise."

"People understand that no good treatment currently exists after their cancer spreads. Everyone wants to know what their risk is for metastasis," said coauthor Annette Stanton, UCLA professor of psychology, psychiatry and biobehavioral sciences. "If the risk is low, it's a huge relief and emotional burden off patients' shoulders. If the risk is high, it enables patients to plan arrangements for their family and finances and make the most of their time alive."

The UCLA survey also measured quality of life and depression symptoms in patients who received genetic test results and compared their rankings to those of untested patients.

"Regardless of their test result, all of the patients rated themselves about the same in terms of quality of life and emotional well-being," said Stanton, who is also a Jonsson Cancer Center member. "We hope that these findings reduce clinical resistance and pave the way for prognostic testing to become the standard of care in the management of ocular melanoma."

"The issue of genetic testing has been a huge source of clinical controversy," said McCannel. "People want information; they have a lot of things they still want to do in life. Knowing their prognosis offers a tool that helps them plan their lives. Our research demonstrates that it's valuable to give people these details, even when their disease is not presently treatable."

"Our results emphasize how important it is for patients to be treated in a full-service hospital research center that offers genetic testing and counseling and treats the whole patient, not just their disease," said Stanton.

Tumor biopsy also helps researchers search for key genes that play a role in aggressive metastasis, improving clinicians' ability to provide the best care.

"After analyzing the tumor specimens, we grow the biopsied cells in a culture dish and can add drugs to test which ones block cancer growth," said McCannel. "That is how we're going to beat this cancer. Developing drugs to target these genes will one day result in therapies and a cure."

The technique of fine-needle aspiration biopsy for collecting cancer cells from the living eye has been utilized at the Jules Stein Eye Institute since 2004, but adopted by only a handful of other ophthalmic centers in the nation.

Although rare, ocular melanoma is the most common eye cancer to strike adults. The National Eye Institute reports some 2,000 newly diagnosed cases of the cancer – roughly seven in 1 million people -- per year. The disease spans the age and ethnic spectrum, and is not hereditary.

*The study's UCLA coauthors included first author Tammy Beran, Dr. Bradley Straatsma and Barry Burgess.*

*The research was supported by funding from the UCLA Jonsson Comprehensive Cancer Center.*

## **Model for new generation of blood vessels challenged**

In-growth and new generation of blood vessels, which must take place if a wound is to heal or a tumor is to grow, have been thought to occur through a branching and further growth of a vessel against a chemical gradient of growth factors. Now a research team at Uppsala University and its University Hospital has shown that mechanical forces are considerably more important than was previously thought. The findings, published today in the journal *Nature Medicine*, open up a new field for developing treatments.

New generation of blood vessels takes place in normal physiological processes, such as when a wound heals, children grow, or the mucous membrane of the womb is built up to be able to receive a fertilized egg. It is also a crucial mechanism in tumor diseases, rheumatism, and certain eye disorders, for example.

How new generation and in-growth of blood vessels takes place has not been fully understood. It has been assumed that the mechanisms are the same as those that occur in embryonic development, which is probably a great over-simplification. The formation of the vascular system in the fetus takes place in a well-organized and reproducible way, which means that we all have blood vessel systems that look very much the same. On the other hand, new generation of vessels in wound healing and tumor growth, for example, occurs in a chaotic environment where it is difficult to see that there would be well-defined gradients of growth factors, and it has not been possible to find evidence of any.

"Unlike these previous models, our findings show that in wound healing, in-growth of new blood vessels takes place via mechanical forces that pull already existing blood vessels into the wound when it heals," says Pär Gerwins, who directed the study and is a physician and interventional radiologist at Uppsala University Hospital as well as a researcher with the Department of Medical Biochemistry and Microbiology at Uppsala University.

It has long been known that specialized connecting tissue cells, so-called myofibroblasts, wander in and pull the wound together. In the study being published it is shown that this wound contraction governs the in-growth of new blood vessels. Since it is a matter, at least initially, of the expansion of already existent blood vessels that have continuous blood circulation, there is a rapid in-growth of fully functional vessels, which is what we see when a wound heals.

The study not only explains a fundamental biological mechanism but also provides clues for new therapeutic goals in treating various diseases. Since myofibroblasts exist in relatively large numbers in tumors and rheumatic joints, one potential strategy to try to block the contractive capacity of these connective tissue cells. The new model can also partially explain why treatment of tumor diseases with blood-vessel inhibiting substances has not been as successful as was hoped.

Finally, the model can partially explain the mechanism behind the positive effect of "vacuum-assisted wound closure," (VAC). This is a method of treatment for hard-to-heal wounds where an air-tight bandage is applied and then the pressure is reduced in the wound with the aid of suction, which creates a continuous mechanical pull in the underlying tissue. Blood-vessel-rich wound-healing tissue is thereby generated much more rapidly, which substantially hastens healing. It is hoped that it will now be possible to understand why some wounds do not heal and also to develop new types of wound treatment.

## **Endless original, copyright-free music**

UGR researchers Miguel Delgado, Waldo Fajardo and Miguel Molina decided to design a software programme that would enable a person who knew nothing about composition to create music. The system they devised, using AI, is called Inmamusys, an acronym for Intelligent Multiagent Music System, and is able to compose and play music in real time.

If successful, this prototype, which has been described recently in the journal *Expert Systems with Applications*, looks likely to bring about great changes in terms of the intrusive and repetitive canned music played in public places.

Miguel Molina, lead author of the study, tells SINC that while the repertoire of such canned music is very limited, the new invention can be used to create a pleasant, non-repetitive musical environment for anyone who has to be within earshot throughout the day.

Everyone's ears have suffered the effects of repetitively-played canned music, be it in workplaces, hospital environments or during phone calls made to directory inquiries numbers. On this basis, the research team decided that it would be "very interesting to design and build an intelligent system able to generate music automatically, ensuring the correct degree of emotiveness (in order to manage the environment created) and originality (guaranteeing that the tunes composed are not repeated, and are original and endless)".

Inmamusys has the necessary knowledge to compose emotive music through the use of AI techniques. In designing and developing the system, the researchers worked on the abstract representation of the concepts

necessary to deal with emotions and feelings. To achieve this, Molina says, "we designed a modular system that includes, among other things, a two-level multiagent architecture".

A survey was used to evaluate the system, with the results showing that users are able to identify the type of music composed by the computer. A person with no musical knowledge whatsoever can use this artificial musical composer, because the user need do nothing more than decide on the type of music".

Beneath the system's ease of use, Miguel Molina reveals that a complex framework is at work to allow the computer to imitate a feature as human as creativity. Aside from creativity, music also requires specific knowledge.

According to Molina, this "is usually something done by human beings, although they do not understand how they do it. In reality, there are numerous processes involved in the creation of music and, unfortunately, we still do not understand many of them. Others are so complex that we cannot analyse them, despite the enormous power of current computing tools. Nowadays, thanks to the advances made in computer sciences, there are areas of research – such as artificial intelligence – that seek to reproduce human behaviour. One of the most difficult facets of all to reproduce is creativity".

### **Farewell to copyright payments**

Commercial development of this prototype will not only change the way in which research is carried out into the relationship between computers and emotions, the means of interacting with music and structures by which music is composed in the future. It will also serve, say the study's authors, to reduce costs.

According to the researchers, "music is highly present in our leisure and working environments, and a large number of the places we visit have canned music systems. Playing these pieces of music involves copyright payments. Our system will make these music copyright payments a thing of the past".

*References: Miguel Delgado; Waldo Fajardo; Miguel Molina-Solana. "Inmamusys: Intelligent multiagent music system". Expert Systems with Applications. número 36, páginas 4574-4580, 2009.*

### **Genes help us make sweet music together**

MUSICAL ability is linked to gene variants that help control social bonding. The finding adds weight to the notion that music developed to cement human relationships.

Irma Järvelä of the University of Helsinki, Finland, and her colleagues recruited people from 19 families with at least one professional musician in each and tested their aptitudes for distinguishing rhythm, pitch and musical pattern. These abilities - which are thought to be innate and unteachable - ran in families, consistent with their being under genetic control.

When the researchers scanned the volunteers' genes, they found that two variants of the gene AVPR1A correlated strongly with musical ability (PLoS One, DOI: 10.1371/journal.pone.0005534). AVPR1A codes for a receptor for the hormone arginine vasopressin and has been linked with bonding, love and altruism in people.

Järvelä thinks musical aptitude evolved because musical people were better at forming attachments to others: "Think of lullabies, which increase social bonding and possibly the survival of the baby."

### **Scientists explain how 'death receptors' designed to kill our cells may make them stronger**

***A review article published in the FASEB Journal shows that death receptors may be prime therapeutic targets for treating a wide variety of cancers, immune disorders and tissue injuries***

It turns out that from the perspective of cell biology, Nietzsche may have been right after all: that which does not kill us does make us stronger. In a review article published in the June 2009 print issue of The FASEB Journal (<http://www.fasebj.org>), scientists from the Mayo Clinic explain how cell receptors (called "death receptors") used by the body to shut down old, diseased, or otherwise unwanted cells (called "apoptosis") may also be used to make cells heartier when facing a wide range of illnesses, from liver disease to cancer.

"Increasing our knowledge of how death receptors function will allow us to develop better and more effective therapies for several human diseases," said Gregory J. Gores, M.D., Chair of the Division of Gastroenterology and Hepatology at the Mayo Clinic in Rochester, Minn., and one of the scientists involved in the work.

In their article, Gores and his colleague, Maria Guicciardi, also from the Mayo Clinic, described the various molecular pathways activated by death receptors and the proteins involved in the process. Specifically, they looked at how these proteins interact with each other and how they redistribute within a cell. Death receptors are an essential tool for the immune system to eliminate cells that have been overtaken by viruses, undergone potentially harmful genetic modifications, or have become too old to function properly. Understanding the exact sequence of events that occurs after death receptors are activated, including identifying key proteins involved in the processes, may allow researchers to develop entirely new therapeutics. These therapeutics not

only would give doctors the ability to choose when and if certain cells are taken out of service, but they would also give doctors the ability to trigger cells to shift into "survival mode."

"As far as names are concerned, nothing in biology sounds more intimidating than 'death receptors,'" said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "Fortunately for us, when scientists look at the intricate machinery of how cells die, they dig up clues to longer, healthier lives."

### **Wet ear wax and unpleasant body odors signal breast cancer risk**

***New research in the FASEB Journal shows that a "breast cancer gene" causes osmidrosis and makes earwax wet and sticky***

If having malodorous armpits (called osmidrosis) and goopy earwax isn't bad enough, a discovery by Japanese scientists may add a more serious problem for women facing these cosmetic calamities. That's because they've found that a gene responsible for breast cancer causes these physical symptoms. The report describing this finding is featured on the cover of The FASEB Journal's June 2009 print issue (<http://www.fasebj.org>), and should arm physicians with another clue for detecting breast cancer risk.

"We do strongly hope that our study will provide a new tool for better predication of breast cancer risk by genotyping," said Toshihisa Ishikawa, Ph.D., a professor from the Department of Biomolecular Engineering at the Tokyo Institute of Technology and the senior researcher involved in the work. "Using a rapid and cost-effective typing method presented in this study would provide a practical tool for pharmacogenomics-based personalized medicine."

To draw their conclusions, Ishikawa and colleagues monitored the activities of a protein created by a gene associated with breast cancer, called "ABCC11." By studying this gene and its complex cellular and molecular interactions in the body, the researchers discovered a distinct link between the gene and excessively smelly armpits and wet, sticky earwax. Specifically, the researchers expressed the ABCC11 gene and variant proteins in cultured human embryonic kidney cells and showed exactly how the ABCC11 gene produces the wet-type earwax and excessive armpit odor. This discovery could lead to practical tools for clinicians—especially those in developing nations—to rapidly identify who may have a higher risk for breast cancer.

"Wet, sticky earwax might not be easily noticed, but most people can't miss unpleasant body odors," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal, "As it turns out, the type of ear wax one has is linked to a gene that leads to bad odors from one's armpit. These may become lifesaving clues to the early detection and treatment of breast cancer."

### **Long odds on space viruses seeding life**

**\* 01 June 2009 by Anil Ananthaswamy**

LIFE on Earth is unlikely to have come from space, says a new study on viruses. If life is ever found on another planet, however, the findings could help us judge whether it arrived from space or not.

Panspermia is the idea that life was seeded by extraterrestrial microbes in the form of hardy bacterial spores that hitched a ride on a space rock and landed on Earth. Jaana Bamford of the University of Jyväskylä in Finland and her colleagues say the key to testing this theory lies with viruses, which are thought to be tied to key steps in the evolution of complex life on Earth.

To find the likelihood of viruses stowing away in spores, the team induced a colony of bacteria hosting the Bam35 virus to form spores. Of the 83 spores that were revived to create new bacterial colonies, only 23 contained the virus (International Journal of Astrobiology, DOI: 10.1017/s1473550409004479).

This result suggests that, whatever the odds of a spore-laden meteoroid going from one planet to another, the odds of viruses hitchhiking within the bacterial spores are much longer, says team member Matti Jalasvuori.

Even if the odd virus did come along from space, it does not explain the huge diversity of viruses on Earth. Unlike cellular organisms, which are all thought to have had one ancestor, viruses are descended from more than one ancestral strain, so it is unlikely that enough virus-laden meteorites landed to seed the "virosphere" we know today. It also makes it unlikely that life on Earth itself came from space. "If life on Earth was because of panspermia, we would probably see a less diverse virosphere," says Jalasvuori.

Even if the odd virus did come from space, it does not explain the huge diversity on Earth

If we find life elsewhere, he adds, the absence of a diverse virosphere could suggest that life on Mars, say, might have originated in panspermia.

Tom Ray, an ecologist at the University of Oklahoma in Norman says the arguments are "plausible, not definitive". He believes that viral complexity on Earth could have evolved however viruses originated. "If viruses quickly emerge after the appearance - either by local origin or panspermia - of cellular life, it would probably be difficult to distinguish between the two cases billions of years later."

## Newly discovered reactions from an old drug may lead to new antibiotics

A mineral found at health food stores could be the key to developing a new line of antibiotics for bacteria that commonly cause diarrhea, tooth decay and, in some severe cases, death.

The trace mineral selenium is found in a number of proteins in both bacterial cells and human cells called selenoproteins. University of Central Florida Associate Professor William Self's research shows that interrupting the way selenoproteins are made can halt the growth of the super bug *Clostridium difficile* and *Treponema denticola*, a major contributor to gum disease.

Infections of *Clostridium difficile* (commonly known as C-diff) lead to a spectrum of illnesses ranging from severe diarrhea to colitis, which can cause death. It's a life-threatening problem in hospitals and nursing homes worldwide, and the number of cases is on the rise. There are an estimated 500,000 cases per year in the United States alone. Between 15,000 to 20,000 people die each year while infected with this superbug. *Treponema denticola* is one of leading causes of gum disease and costs individuals thousands of dollars in dental care each year.

Self's findings are published in the May and June editions of the *Journal of Biological Inorganic Chemistry* and the *Journal of Bacteriology*. The National Institutes of Health and the Florida Department of Health funded the research, which was conducted at UCF during the past three years.

"It's the proof of principle that we are excited about," Self said from his research lab at UCF. "No one has ever tried this approach, and it could potentially be a source for new narrow spectrum antibiotics that block bacteria that require selenium to grow."

The key discovery occurred when the team found that the gold drug Auranofin, used to treat arthritis, impacted selenium's metabolism process. The chemical reaction changes the selenium, which prevents bacteria from using it to grow. Auranofin is an FDA-approved gold salt compound that is used to control inflammation and is already known to inhibit the activity of certain selenoproteins. Since certain bacteria, such as *C. difficile*, require selenoproteins for energy metabolism, the drug acts as a potent antimicrobial halting the growth of the bacteria.

The initial studies with *C. difficile* led to studies with *T. denticola*, known for several years to require selenium for growth. While testing the gold salt, Self's group also uncovered another surprise; the stannous salts found in many antimicrobial toothpastes in the form of stannous fluoride also inhibited the synthesis of selenoproteins. Previous independent research had already established that stannous salts are more effective at preventing tooth decay and inhibiting growth of *T. denticola*, but the mechanism of this inhibition of growth was not yet known. These findings could lead to new approaches to preventing gum disease.

"No one has tried to block the metabolism of selenium before as a therapeutic approach," Self said. "That's what's new and exciting and could lead to a whole host of other possibilities, including a better understanding of how the gold salt works for arthritis."

Self said more research is needed, and he already has another grant proposal before the NIH that would move his research forward.

## Squid 'sight': Not just through eyes

MADISON — It's hard to miss the huge eye of a squid. But now it appears that certain squids can detect light through an organ other than their eyes as well. That's what researchers at the University of Wisconsin-Madison report in the current issue (June 2) of the *Proceedings of the National Academy of Sciences*.

The study shows that the light-emitting organ some squids use to camouflage themselves to avoid being seen by predators - usually fish sitting on the ocean floor - also detects light. The findings may lead to future studies that provide insight into the mechanisms of controlling and perceiving light.

"Evolution has a 'toolkit' and when it needs to do a particular job, such as see light, it uses the same toolkit again and again," explains lead author Margaret McFall-Ngai, a professor of medical microbiology and immunology at the UW-Madison School of Medicine and Public Health (SMPH). "In this case, the light organ, which comes from different tissues than the eye during development, uses the same proteins as the eye to see light."

In studying the squid for the past 20 years, McFall-Ngai and her colleagues have been drawn to the fact that the squid-light organ is a natural model of symbiosis - an interdependent relationship between two different species in which each benefits from the other.

In this case, the light organ is filled with luminous bacteria that emit light and provide the squid protection against predators. In turn, the squid provides housing and nourishment for the bacteria.

The UW-Madison researchers have been intrigued by the light organ's "counterillumination" ability — this capacity to give off light to make squids as bright as the ocean surface above them, so that predators below can't see them.

"Until now, scientists thought that illuminating tissues in the light organ functioned exclusively for the control of the intensity and direction of light output from the organ, with no role in light perception," says McFall-Ngai. "Now we show that the *E. scolopes* squid has additional light-detecting tissue that is an integral component of the light organ."

The researchers demonstrated that the squid light organ has the molecular machinery to respond to light cues. Molecular analysis showed that genes that produce key visual proteins are expressed in light-organ tissues, including genes similar to those that occur in the retina. They also showed that, as in the retina, these visual proteins respond to light, producing a physiological response.

"We found that the light organ in the squid is capable of sensing light as well as emitting and controlling the intensity of luminescence," says co-author Nansi Jo Colley, SMPH professor of ophthalmology and visual sciences and of genetics.

Adds McFall-Ngai, "The tissues may perceive environmental light, providing the animal with a mechanism to compare this light with its own light emission."

McFall-Ngai's large research program into the relatively simple squid-light organ symbiosis aims to shed light on symbiosis affecting humans.

"We know that humans house trillions of bacteria associated with components of eight of their 10 organ systems," she says. "These communities of bacteria are stable partners that make us healthy."

### **CU-Boulder study shows 53-million-year-old high Arctic mammals wintered in darkness**

Ancestors of tapirs and ancient cousins of rhinos living above the Arctic Circle 53 million years ago endured six months of darkness each year in a far milder climate than today that featured lush, swampy forests, according to a new study led by the University of Colorado at Boulder.

CU-Boulder Assistant Professor Jaelyn Eberle said the study shows several varieties of prehistoric mammals as heavy as 1,000 pounds each lived on what is today Ellesmere Island near Greenland on a summer diet of flowering plants, deciduous leaves and aquatic vegetation. But in winter's twilight they apparently switched over to foods like twigs, leaf litter, evergreen needles and fungi, said Eberle, curator of fossil vertebrates at the University of Colorado Museum of Natural History and chief study author.

The study has implications for the dispersal of early mammals across polar land bridges into North America and for modern mammals that likely will begin moving north if Earth's climate continues to warm. A paper on the subject co-authored by Henry Fricke of Colorado College in Colorado Springs and John Humphrey of the Colorado School of Mines in Golden appears in the June issue of *Geology*.

The team used an analysis of carbon and oxygen isotopes extracted from the fossil teeth of three varieties of mammals from Ellesmere Island -- a hippo-like, semi-aquatic creature known as *Coryphodon*, a second, smaller ancestor of today's tapirs and a third rhino-like mammal known as *brontothere*. Animal teeth are among the most valuable fossils in the high Arctic because they are extremely hard and better able to survive the harsh freeze-thaw cycles that occur each year, Eberle said.

Telltale isotopic signatures of carbon from enamel layers that form sequentially during tooth eruption allowed the team to pinpoint the types of plant materials consumed by the mammals as they ate their way across the landscape through the seasons, Eberle said.



*A hippo-like mammal known as Coryphodon was one of several ancient mammal groups that endured twilight winters in the high Arctic 53 million year ago, according to a new study led by the University of Colorado at Boulder. Image copyright American Museum of Natural History/D. Finnin.*

"We were able to use carbon signatures preserved in the tooth enamel to show that these mammals did not migrate or hibernate," said Eberle. "Instead, they lived in the high Arctic all year long, munching on some unusual things during the dark winter months." The study was funded by the National Science Foundation.

An analysis of oxygen isotopes from the fossil teeth helped determine seasonal changes in surface drinking water tied to precipitation and temperature, providing additional climate information, said Eberle. The results point to warm, humid summers and mild winters in the high Arctic 53 million years ago, where temperatures probably ranged from just above freezing to near 70 degrees Fahrenheit, Eberle said.

The environment on central Ellesmere Island, located at about 80 degrees north latitude, was part of a much larger circumpolar Arctic region at the time, she said. It probably was similar to swampy cypress forests in the southeast United States today and still contains fossil tree stumps as large as washing machines, Eberle said.

On central Ellesmere Island in today's high Arctic -- a polar desert that features tundra, permafrost, ice sheets, sparse vegetation and a few small mammals -- the temperature ranges from roughly minus 37 degrees F in winter to 48 degrees F in summer and is the coldest, driest environment on Earth. There is no sunlight in the high Arctic between October and February, and the midnight sun is present from mid-April through the end of August.

The year-round presence of mammals such as the hippo-like *Coryphodon*, tapirs and brontotheres in the high Arctic was a "behavioral prerequisite" for their eventual dispersal across high-latitude land bridges that geologists believe linked Asia and Europe with North America, Eberle said. Their dietary chemical signatures, portly shapes and fossil evidence for babies and juveniles in the Arctic preclude the idea of long, seasonal migrations to escape the winter darkness, she said.

"In order for mammals to have covered the great distances across land bridges that once connected the continents, they would have required the ability to inhabit the High Arctic year-round in proximity to these land bridges," Eberle said.

Instead, the animals likely made their way south from the Arctic in minute increments over millions of years as the climate shifted. "This study may provide the behavioral smoking gun for how modern groups of mammals like ungulates -- ancestors of today's horses and cattle -- and true primates arrived in North America," said Eberle, also an assistant professor in CU-Boulder's geological sciences department.

The surprising menagerie of Arctic creatures during the early Eocene epoch, which lasted from roughly 50 million to 55 million years ago, first became evident in 1975 when a team led by Mary Dawson of the Carnegie Museum of Natural History in Pittsburgh discovered fossil alligator jaw bones. Since then, fossils of aquatic turtles, giant tortoises, snakes and even flying lemurs -- one of the earliest forms of primates -- have been found on Ellesmere Island, said Eberle.

The new Geology study also foreshadows the impacts of continuing global warming on Arctic plants and animals, Eberle said. Temperatures in the Arctic are rising twice as fast as those at mid-latitudes as greenhouse gases build up in Earth's atmosphere from rising fossil-fuel burning, and air temperatures over Greenland have risen by more than 7 degrees F since 1991, according to climate scientists.

"We are hypothesizing that lower-latitude mammals will migrate north as the temperatures warm in the coming centuries and millennia," she said. If temperatures ever warm enough in the future to rival the Eocene, there is the possibility of new intercontinental migrations by mammals."

Because the oldest known tapir fossils are from the Arctic, there is the possibility that some prehistoric mammals could have evolved in the circumpolar Arctic and then dispersed through Asia, Europe and North America, said Eberle. "We may have to re-think the world of the early Eocene, when all of the Arctic land masses were connected in a supercontinent of sorts," she said.

### **Drug's epilepsy-prevention effect may be widely applicable**

A drug with potential to prevent epilepsy caused by a genetic condition may also help prevent more common forms of epilepsy caused by brain injury, according to researchers at Washington University School of Medicine in St. Louis.

Scientists found that the FDA-approved drug rapamycin blocks brain changes believed to cause seizures in rats. In a paper last year, the same group showed that rapamycin prevents brain changes in mice triggered by one of the most common genetic causes of epilepsy, tuberous sclerosis (TS).

"We hope to shift the focus from stopping seizures to preventing the brain abnormalities that cause seizures in the first place, and our results in the animal models so far have been encouraging," says senior author Michael Wong, M.D., Ph.D. The study was published in *The Journal of Neuroscience* on May 27.

One percent of the population has epilepsy, which can result from genetic mutations, brain injuries and environmental insults. According to Wong, one-third of that group does not respond well to current anti-seizure medications.

"Researchers have traditionally tested potential epilepsy drugs on animals that were already having seizures," Wong says. "We may be able to improve our success rate by stepping back a little and trying to find a treatment that can halt the disease process prior to the start of seizures."

In earlier studies of TS, Wong and others showed that proteins involved in TS overactivate mTOR (mammalian target of rapamycin), a powerful regulatory protein. Wong speculated that mTOR might influence proteins involved in communication between brain cells, which could explain why TS causes seizures.



To test the theory, he gave rapamycin to mice with a TS gene mutation. The drug binds to mTOR, reducing its ability to activate other genes and proteins. Mice that received the drug were seizure-free and lived longer.

For the new study, Ling-Hui Zeng, Ph.D., a postdoctoral fellow, studied an animal model of epilepsy created by giving rats a drug known as kainate. Exposure to the drug initially causes a prolonged seizure. A few days later, the rats begin having spontaneous seizures. Research has previously shown that kainate causes brain cell death and the creation of new brain cells, and that some surviving brain cells grow multiple new branches, a phenomenon called mossy fiber sprouting. Scientists have speculated that this new and erratic growth of nerve cell branches may help promote the continuous chaotic nerve cell firing that takes place during seizures.

Zeng began her studies by showing that kainate causes an increase in a marker for mTOR activity during the initial seizure; this increase returned as rats began to develop spontaneous seizures days later and suggested that rapamycin might help prevent brain changes that underlie seizures.

When Zeng gave the rats rapamycin prior to kainate, the rats still had the initial seizure, but brain cell death, new brain cells and mossy fiber sprouting all decreased, and the later spontaneous seizures were also significantly reduced. Rats that received rapamycin after the initial seizure caused by kainate still lost and gained brain cells, but they had less mossy fiber sprouting and experienced fewer subsequent seizures.

"The fact that rapamycin had beneficial effects even after the first seizure is particularly exciting, because it suggests that if similar phenomena occur in the human brain, treating patients with mTOR inhibitors after a brain injury might reduce the chances of developing epilepsy," says Wong. "This may be particularly important for the surge of veterans returning with traumatic brain injuries from Iraq and Afghanistan."

Rapamycin is currently being evaluated in clinical trials as a treatment for the brain tumors caused by TS. Wong believes the new paper will add impetus for trials to test rapamycin and other mTOR inhibitors as epilepsy prevention drugs.

*Zeng L-H, Rensing NR, Wong M. The mammalian target of rapamycin signaling pathway mediates epileptogenesis in a model of temporal lobe epilepsy. The Journal of Neuroscience, May 27, 2009.*

### **Cost shifting may make arthritis medications too expensive for medicare beneficiaries** **News from Arthritis Care & Research**

Biologic disease-modifying antirheumatic drugs (DMARDs) such as adalimumab, etanercept and infliximab are effective at reducing symptoms and slowing progression of rheumatoid arthritis (RA). These drugs act more quickly, require less laboratory monitoring, and are better tolerated than nonbiologic DMARDs, but they are also up to 100 times more expensive. Insurance plans differ greatly in their coverage of and cost sharing for biologic DMARDs, sometimes shifting a large portion of the cost of patients. A new study examined the cost-sharing structures for biologic DMARDs in Part D plans and the resulting cost burden to patients. The study was published in the June issue of *Arthritis Care & Research* (<http://www3.interscience.wiley.com/journal/77005015/home>).

In 2003, Congress created the Medicare Replacement Drug Demonstration (MRDD) to provide temporary drug insurance until the start of Medicare Part D in 2006. The MRDD, which ran September 2004 – December 2005, targeted low-income vulnerable Medicare patients with select conditions, including RA, who did not have comprehensive drug insurance coverage. This program had similar cost-sharing arrangements to Medicare Part D and evaluations showed that it reduced financial barriers and improved health outcomes. However, unlike the MRDD, Part D plans could place high-cost items such as biologic DMARDs in a specialty tier, where they are subject to higher patient cost sharing. There is concern that specialty tiering imposes a heavy financial burden on RA patients.

Led by Jennifer M. Polinski of Brigham and Women's Hospital in Boston, researchers followed almost 15,000 vulnerable, low-income patients who were enrolled in the MRDD as they transitioned into Part D in 2006. They grouped patients into one of three drug coverage options: enrollment in a Part D plan further stratified by a Medicare Advantage or stand-alone plan, other creditable coverage or unknown coverage. They examined the benefit design of each plan, as well as potential differences in beneficiaries' annual out-of-pocket costs for biologic DMARDs under three coverage scenarios.

They found that 81 percent of poor and disabled Medicare beneficiaries with RA who participated in the MRDD program had enrolled in Part D plans by July 2006. Compared with stand-alone Part D plans, Medicare Advantage plans offered lower deductibles, lower premiums, and were more likely to require copayments (which are fixed), rather than coinsurance (typically a percentage paid by the insured person pays after an insurance deductible has been exceeded). They also placed significantly fewer restrictions on biologic DMARD reimbursement. "In spite of the greater generosity and lesser restrictions of Medicare Advantage plans, the most sick and most financially needy patients enrolled in these plans less often than they did in stand-alone plans," the authors note.

Most patients enrolled in plans that placed biologic DMARDs on high-cost specialty tiers and used coinsurance proportions as high as 75 percent. The specialty tier was created to ensure that beneficiaries receiving high-cost biologic agents were not discriminated against in terms of cost sharing, but there is concern about the financial impact of this structure, especially the widespread use of high coinsurance. The study found that Part D plans that require coinsurance instead of copayments shift the financial burden of these high-cost medications from the plan to the patient and to Medicare. In plans where cost sharing is high (e.g. plans with high coinsurance), patients may delay or not even begin therapy due to the high cost; in plans with cost sharing that is steep but manageable (e.g. plans with high copayments) patients may begin therapy but then discontinue it when faced with paying the full cost of the medication out of pocket. "Neither scenario is optimal for patients who may benefit from biologic DMARDs," the authors point out.

Specialty tier and coinsurance resulted in estimated annual expenditures for patients that exceeded \$4,000 despite drug insurance coverage and more Part D plans have adopted specialty tiering over time. In 2006, 60 percent of the national stand-alone plans used this system but by 2008, 87 percent were using it. Similarly, between 2006 and 2008 the number of plans charging 33 percent coinsurance increased more than five-fold. "Patients assume up to 28 percent and Medicare assumes more than 58 percent of the costs of biologic DMARDs in our scenarios, yet neither is in a position to sustain such financial burden," the authors conclude. "As more biologic DMARDs are approved and used for RA and more plans use the specialty tier system, both beneficiaries and Medicare face costs they may be increasingly unable to afford."

*Article: "Impact of Medicare Part D on Access to and Cost Sharing for Specialty Biologic Medications for Beneficiaries with Rheumatoid Arthritis," Jennifer M. Polinski, Penny E. Mohr, Lorraine Johnson, Arthritis & Rheumatism (Arthritis Care & Research), June 2009.*

### **Improved DNA stool test could detect digestive cancers in multiple organs**

ROCHESTER, Minn. -- Mayo Clinic researchers have demonstrated that a noninvasive screening test can detect not only colorectal cancer but also the common cancers above the colon -- including pancreas, stomach, biliary and esophageal cancers. This is one of more than 100 Mayo Clinic studies being presented at Digestive Disease Week 2009 in Chicago, May 30 – June 4.

Gastrointestinal (GI) cancers account for approximately one in four cancer deaths. While high cure rates can be achieved with early-stage detection for each type, only colorectal cancer is currently screened at the population level. Most people associate colorectal cancer screening with invasive colonoscopy, but previous Mayo Clinic research has shown that stool DNA testing can identify both early-stage colorectal cancer and precancerous polyps. Researchers are now studying the use of noninvasive stool DNA testing to detect lesions and cancer throughout the GI tract.

"Patients are often worried about invasive tests like colonoscopies, and yet these tests have been the key to early cancer detection and prevention," says David Ahlquist, M.D., Mayo Clinic gastroenterologist and lead researcher on the study. "Our research team continues to look for more patient-friendly tests with expanded value, and this new study reveals an opportunity for multi-organ digestive cancer screening with a single noninvasive test."

The researchers studied 70 patients with cancers throughout the digestive tract. Besides colon cancer, the study looked at throat, esophagus, stomach, pancreatic, bile duct, gallbladder and small bowel cancers to determine if gene mutations could be detected in stool samples. Using a stool test approach developed at Mayo Clinic, researchers targeted DNA from cells that are shed continuously from the surface of these cancers. Also studied were 70 healthy patients. Stool tests were performed on cancer patients and healthy controls by technicians unaware of sample source. The stool DNA test was positive in nearly 70 percent of digestive cancers but remained negative for all healthy controls, thus demonstrating the approach's feasibility.

Stool DNA testing detected cancers at each organ site, including 65 percent of esophageal cancers, 62 percent of pancreatic cancers, and 75 percent of bile duct and gallbladder cancers. In this series, 100 percent of both stomach and colorectal cancers were detected. Importantly, stool test results did not differ by cancer stage; early-stage cancers were just as likely to be detected as late-stage cancers.

"It's very exciting to see this level of sensitivity for digestive cancer detection in our first look at this test application," says Dr. Ahlquist, "Historically, we've approached cancer screening one organ at a time. Stool DNA testing could shift the strategy of cancer screening to multi-organ, whole-patient testing and could also open the door to early detection of cancers above the colon which are currently not screened. The potential impact of this evolution could be enormous."

In October 2008, this Mayo Clinic research team published results of a multicenter study using first-generation stool DNA testing. In the seven-year, multicenter study (Ann Intern Med 2008;149:441-50), researchers found that the first-generation stool DNA tests were better than fecal blood tests for detecting

cancer and precancerous polyps of the colon. In January 2009 (*Gastroenterology* 2009;136:459-70), Mayo researchers published some technical improvements that nearly doubled the sensitivity of stool DNA testing for detecting premalignant polyps and increased cancer detection to about 90 percent, which is the approximate rate of detection observed for CT colonography.

Researchers hope that the next generation tests will have significant improvements in accuracy, processing speed, ease of patient use and affordability. "We anticipate that next generation tests will also be able to predict the tumor site, which will help physicians direct diagnostic studies and minimize unnecessary procedures," says Dr. Ahlquist.

*Dr. Ahlquist and Mayo Clinic have a financial interest related to technology studied in this research.*

*Other researchers from Mayo Clinic include: Hongzhi Zou, M.D., Ph.D.; Jonathan Harrington; William Taylor; Mary Devens; Xiaoming Cao, M.D.; Russell Heigh, M.D.; Yvonne Romero, M.D.; Suresh Chari, M.D.; Gloria Petersen, Ph.D.; Lewis Roberts, M.B.Ch.B., Ph.D.; Jan Kasperbauer, M.D.; Julie Simonson; David I. Smith, Ph.D.; and Thomas Smyrk, M.D.*

### **World first: Chinese scientists create pig stem cells**

#### ***Discovery has far-reaching implications for animal and human health***

Scientists have managed to induce cells from pigs to transform into pluripotent stem cells – cells that, like embryonic stem cells, are capable of developing into any type of cell in the body. It is the first time in the world that this has been achieved using somatic cells (cells that are not sperm or egg cells) from any animal with hooves (known as ungulates).

The implications of this achievement are far-reaching; the research could open the way to creating models for human genetic diseases, genetically engineering animals for organ transplants for humans, and for developing pigs that are resistant to diseases such as swine flu.

The work is the first research paper to be published online today (Wednesday 3 June) in the newly launched *Journal of Molecular Cell Biology* [1].

Dr Lei Xiao, who led the research, said: "To date, many efforts have been made to establish ungulate pluripotent embryonic stem cells from early embryos without success. This is the first report in the world of the creation of domesticated ungulate pluripotent stem cells. Therefore, it is entirely new, very important and has a number of applications for both human and animal health."

Dr Xiao, who heads the stem cell lab at the Shanghai Institute of Biochemistry and Cell Biology (Shanghai, China), and colleagues succeeded in generating induced pluripotent stem cells by using transcription factors to reprogramme cells taken from a pig's ear and bone marrow. After the cocktail of reprogramming factors had been introduced into the cells via a virus, the cells changed and developed in the laboratory into colonies of embryonic-like stem cells. Further tests confirmed that they were, in fact, stem cells capable of differentiating into the cell types that make up the three layers in an embryo – endoderm, mesoderm and ectoderm – a quality that all embryonic stem cells have. The information gained from successfully inducing pluripotent stem cells (iPS cells) means that it will be much easier for researchers to go on to develop embryonic stem cells (ES cells) that originate from pig or other ungulate embryos.

Dr Xiao said: "Pig pluripotent stem cells would be useful in a number of ways, such as precisely engineering transgenic animals for organ transplantation therapies. The pig species is significantly similar to humans in its form and function, and the organ dimensions are largely similar to human organs. We could use embryonic stem cells or induced stem cells to modify the immune-related genes in the pig to make the pig organ compatible to the human immune system. Then we could use these pigs as organ donors to provide organs for patients that won't trigger an adverse reaction from the patient's own immune system.

"Pig pluripotent stem cell lines could also be used to create models for human genetic diseases. Many human diseases, such as diabetes, are caused by a disorder of gene expression. We could modify the pig gene in the stem cells and generate pigs carrying the same gene disorder so that they would have a similar syndrome to that seen in human patients. Then it would be possible to use the pig model to develop therapies to treat the disease.

"To combat swine flu, for instance, we could make a precise, gene-modified pig to improve the animal's resistance to the disease. We would do this by first, finding a gene that has anti-swine flu activity, or inhibits the proliferation of the swine flu virus; second, we can introduce this gene to the pig via pluripotent stem cells – a process known as gene 'knock-in'. Alternatively, because the swine flu virus needs to bind with a receptor on the cell membrane of the pig to enter the cells and proliferate, we could knock out this receptor in the pig via gene targeting in the pig induced pluripotent stem cell. If the receptor is missing, the virus will not infect the pig."

In addition to medical applications for pigs and humans, Dr Xiao said his discovery could be used to improve animal farming, not only by making the pigs healthier, but also by modifying the growth-related genes to change and improve the way the pigs grow.

However, Dr Xiao warned that it could take several years before some of the potential medical applications of his research could be used in the clinic.

The next stage of his research is to use the pig iPS cells to generate gene-modified pigs that could provide organs for patients, improve the pig species or be used for disease resistance. The modified animals would be either "knock in" pigs where the iPS or ES cells have been used to transfer an additional bit of genetic material (such as a piece of human DNA) into the pig's genome, or "knock out" pigs where the technology is used to prevent a particular gene functioning.

Commenting on the study, the journal's editor-in-chief, Professor Dangsheng Li, said: "This research is very exciting because it represents the first rigorous demonstration of the establishment of pluripotent stem cell in ungulate species, which will open up interesting opportunities for creating precise, gene-modified animals for research, therapeutic and agricultural purposes."

[1] *Generation of pig induced pluripotent stem cells with a drug-inducible system. Journal of Molecular Cell Biology. doi:10.1093/jmcb/jmp003*

### **Bleeding disorders going undiagnosed; new guidelines to help**

DURHAM, NC -- Nearly one percent of the population suffers from bleeding disorders, yet many women don't know they have one because doctors aren't looking for the condition, according to researchers at Duke University Medical Center.

That's about to change, now that an international expert consortium specifically outlined the definitive signs that may signal the presence of a bleeding disorder in women. The consortium's recommendations are published online and will appear in the July issue of the American Journal of Obstetrics and Gynecology.

The new guidelines aren't just for doctors. Women who suffer from heavy menstrual cycles should be on the lookout for these signs as well, says Andra James, MD, a Duke obstetrician, who says about 25 percent of women with heavy menstruation may have an undiagnosed bleeding disorder.

"Heavy bleeding should not be ignored," says James, the paper's lead author. "When a woman's blood can't clot normally the most obvious sign is a heavy period."

Yet when faced with these scenarios, most doctors aren't suspecting a blood clotting problem is to blame. "Sometimes they think hormones are the cause, or fibroids," says James. "In some cases they recommend removal of the uterus or offer another gynecologic explanation when the real contributing factor is a blood clotting disorder."

In previous studies, women who ultimately were treated for a bleeding disorder reported waiting 16 years, on average, before being diagnosed. In extreme cases, James says undiagnosed bleeding disorders have led to women bleeding to death during menstruation, childbirth and surgical procedures.

The most common inherited bleeding disorder is von Willebrand disease, says James, author of 100 Questions and Answers About von Willebrand Disease (Jones and Bartlett). Common criteria for diagnosis include the presence of a family history of bleeding, personal history of bleeding and laboratory tests that indicate the lack of a protein called von Willebrand factor which is essential for clotting.

Without the laboratory test, the consortium says women and doctors should be on the lookout for the following:

- \* Heavy blood loss during menstruation
- \* Family history of bleeding disorder
- \* Notable bruising without injury
- \* Minor wound bleeding that lasts more than five minutes
- \* Prolonged or excessive bleeding following dental extraction
- \* Unexpected surgical bleeding
- \* Hemorrhaging that requires blood transfusion
- \* Postpartum hemorrhaging, especially if occurs more than 24 hours after delivery.

"Too often women think heavy bleeding is okay because the women in their family -- who may also have an undiagnosed bleeding disorder -- have heavy periods as well," says James. "We want women who continually experience abnormal reproductive tract bleeding, specifically heavy menstrual bleeding, to be alert to these other signs and approach their physicians about being evaluated."

In addition, she says doctors should be asking the right questions and ordering appropriate laboratory tests in suspected patients.

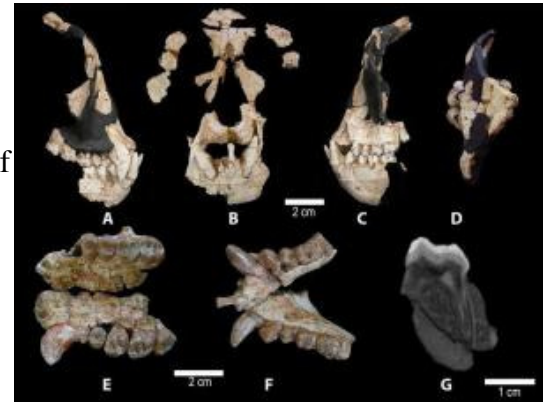
"Not every patient who has abnormal reproductive tract bleeding has a bleeding disorder, and most don't," James says. "But since up to one-quarter do, this needs to be recognized. Once treated, these women can expect to have normal periods and go through childbirth safely."

*The consortium's meeting received financial support from CSL Behring.*

## New Hominid 12 Million Years Old Found In Spain, With 'Modern' Facial Features

ScienceDaily (June 2, 2009) — Researchers have discovered a fossilized face and jaw from a previously unknown hominoid primate genus in Spain dating to the Middle Miocene era, roughly 12 million years ago. Nicknamed "Lluc," the male bears a strikingly "modern" facial appearance with a flat face, rather than a protruding one. The finding sheds important new light on the evolutionary development of hominids, including orangutans, chimpanzees, bonobos, gorillas and humans.

In a study appearing in the Proceedings of the National Academy of Sciences, Salvador Moyà-Solà, director of the Institut Català de Paleontologia (ICP) at the Universitat Autònoma de Barcelona, and colleagues present evidence for the new genus and species, dubbed *Anoiapithecus brevirostris*. The scientific name is derived from the region where the fossil was found (l'Anoia) and also from its "modern" facial morphology, characterized by a very short face.



***The face, jaw and teeth of a 12-million-year-old hominid named *Anoiapithecus brevirostris*. The fossil's presence in Spain suggests that hominids migrated from Europe into Africa before the evolution of modern humans (Image: National Academy of Sciences, PNAS)***

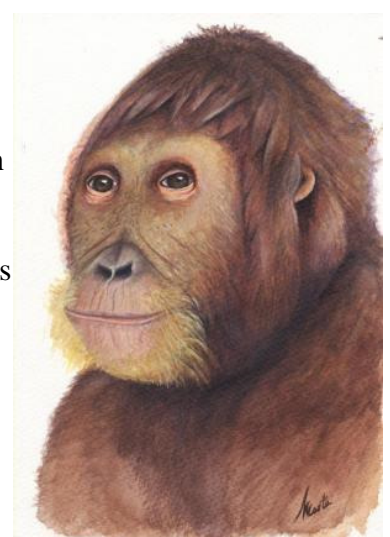
The research team at the ICP also includes collaborator David M. Alba, predoctoral researcher Sergio Almécija, postdoctoral researcher Isaac Casanovas, researcher Meike Köhler, postdoctoral researcher Soledad De Esteban, collaborator Josep M. Robles, curator Jordi Galindo, and predoctoral researcher Josep Fortuny.

Their findings are based on a partial cranium that preserves most of the face and the associated mandible. The cranium was unearthed in 2004 in the fossil-rich area of Abocador de Can Mata (els Hostalets de Pierola, l'Anoia, Barcelona), where remains of other fossilized hominid species have been found. Preparing the fossil for study was a complicated process, due to the fragility of the remains. But once the material was available for analysis, the results were surprising: The specimen (IPS43000) combined a set of features that, until now, had never been found in the fossil record.

*Anoiapithecus* displays a very modern facial morphology, with a muzzle prognathism (i.e., protrusion of the jaw) so reduced that, within the family Hominidae, scientists can only find comparable values within the genus *Homo*, whereas the remaining great apes are notoriously more prognathic (i.e., having jaws that project forward markedly). The extraordinary resemblance does not indicate that *Anoiapithecus* has any relationship with *Homo*, the researchers note. However, the similarity might be a case of evolutionary convergence, where two species evolving separately share common features.

Lluc's discovery may also hold an important clue to the geographical origin of the hominid family. Some scientists have suspected that a group of primitive hominoids known as kenyapithecines (recorded from the Middle Miocene of Africa and Eurasia) might have been the ancestral group that all hominids came from. The detailed morphological study of the cranial remains of Lluc showed that, together with the modern anatomical features of hominids (e.g., nasal aperture wide at the base, high zygomatic rood, deep palate), it displays a set of primitive features, such as thick dental enamel, teeth with globulous cusps, very robust mandible and very procumbent premaxilla. These features characterize a group of primitive hominoids from the African Middle Miocene, known as afropithecids.

Interestingly, in addition to having a mixture of hominid and primitive afropithecid features, Lluc displays other characteristics, such as a very anterior position of the zygomatic, a very strong mandibular torus and, especially, a very reduced maxillary sinus. These are features shared with kenyapithecines believed to have dispersed outside the African continent and colonized the Mediterranean region, by about 15 million years ago.



***Lluc reconstruction. (Credit: Image courtesy of Universitat Autònoma de Barcelona)***

In other words, the researchers speculate, hominids might have originally radiated in Eurasia from kenyapithecine ancestors of African origin. Later on, the ancestors of African great apes and humans would have dispersed again into Africa -- the so-called "into Africa" theory, which remains controversial. However, the authors do not completely rule out the possibility that pongines (orangutans and related forms) and hominines (African apes and humans) separately evolved in Eurasia and Africa, respectively, from different kenyapithecine ancestors.

The project at els Hostalets de Pierola is continuing and, the researchers anticipate, more fossil remains will be found in the future that will provide key information to test their hypotheses.

**Journal reference:**

*I. Salvador Moyà-Solà, David M. Alba, Sergio Almécija, Isaac Casanovas-Vilar, Meike Köhler, Soledad De Esteban-Trivigno, Josep M. Robles, Jordi Galindo, and Josep Fortuny. A unique Middle Miocene European hominoid and the origins of the great ape and human clade. Proceedings of the National Academy of Sciences, 2009; DOI: 10.1073/pnas.0811730106 Adapted from materials provided by Barcelona, Universitat Autònoma de.*

## **Women Faring Well in Hiring and Tenure Processes for Science and Engineering Jobs At Research Universities, But Still Underrepresented in Applicant Pools**

WASHINGTON -- Although women are still underrepresented in the applicant pool for faculty positions in math, science, and engineering at major research universities, those who do apply are interviewed and hired at rates equal to or higher than those for men, says a new report from the National Research Council. Similarly, women are underrepresented among those considered for tenure, but those who are considered receive tenure at the same or higher rates than men.

The congressionally mandated report examines how women at research-intensive universities fare compared with men at key transition points in their careers. Two national surveys were commissioned to help address the issue. The report's conclusions are based on the findings of these surveys of tenure-track and tenured faculty in six disciplines -- biology, chemistry, mathematics, civil engineering, electrical engineering, and physics -- at 89 institutions in 2004 and 2005. The study committee also heard testimony and examined data from federal agencies, professional societies, individual university studies, and academic articles.

In each of the six disciplines, women who applied for tenure-track positions had a better chance of being interviewed and receiving job offers than male applicants had. For example, women made up 20 percent of applicants for positions in mathematics but accounted for 28 percent of those interviewed, and received 32 percent of the job offers. This was also true for tenured positions, with the exception of those in biology.

However, women are not applying for tenure-track jobs at research-intensive universities at the same rate that they are earning Ph.D.s, the report says. The gap is most pronounced in disciplines with larger fractions of women receiving Ph.D.s; for example, while women received 45 percent of the Ph.D.s in biology awarded by research-intensive universities from 1999 to 2003, they accounted for only 26 percent of applicants to tenure-track positions at those schools. Research is needed to investigate why more women are not applying for these jobs, the committee said.

"Our data suggest that, on average, institutions have become more effective in using the means under their direct control to promote faculty diversity, including hiring and promoting women and providing resources," said committee co-chair Claude Canizares, Bruno Rossi Professor of Physics and vice president for research at the Massachusetts Institute of Technology. "Nevertheless, we also find evidence for stubborn and persistent underrepresentation of women at all faculty ranks."

The surveys revealed that most institutional strategies to try to increase the proportion of women in the applicant pool -- such as targeted advertising and recruiting at conferences -- did not show significant effectiveness, the report says. One strategy did appear to make a difference: Having a female chair of the search committee and a high number of women on the committee were associated with a higher number of women in the applicant pool.

The report also assessed gender differences in the following areas:

**Access to institutional resources:** Men and women reported comparable access to many institutional resources, including start-up packages, travel funds, and supervision of similar numbers of postdocs and research assistants. And in general, men and women spent similar proportions of their time on teaching, research, and service. Although at first glance men seemed to have more lab space than women, this difference disappeared when other factors such as discipline and faculty rank were accounted for. However, men appeared to have greater access to equipment needed for research and to clerical support, the report said.

**Tenure:** In every field, women were underrepresented among candidates for tenure relative to the number of female assistant professors. In chemistry, for example, women made up 22 percent of assistant professors, but only 15 percent of the faculty being considered for tenure. Women also spent significantly longer time as assistant professors. However, women who did come up for tenure review were at least as likely as men to receive tenure.

**Salary:** Women full professors were paid on average 8 percent less than their male counterparts, the report says. This difference in salary did not exist in the ranks of associate and assistant professors.

**Climate and interaction with colleagues:** Female faculty reported that they were less likely than men to engage in conversation with their colleagues on many professional topics, including research, salary, and

benefits. This distance may prevent women from accessing important information and may make them feel less included and more marginalized in their professional lives, the committee observed. While on average institutions have done more to address aspects of career transitions under their control, the report notes, one of the remaining challenges may be in the climate at the departmental level.

**Outcomes:** On most key measures -- grant funding, nominations for awards and honors, and offers of positions at other institutions -- there is little evidence of differences in outcomes. In terms of funding for research, male faculty had significantly more funding than female faculty in biology; in other disciplines, the differences were not significant.

The committee urged further research on unanswered questions, such as why more women are not applying for tenure-track positions, why female faculty continue to experience a sense of isolation, and how nonacademic issues affect women's and men's career choices at critical junctures.

"Overall the newly released data indicate important progress, and signal to both young men and especially to young women that what had been the status quo at research-intensive universities is changing," said committee co-chair Sally Shaywitz, Audrey G. Ratner Professor in Learning Development and co-director of the Yale Center for Dyslexia and Creativity, Yale University School of Medicine. "There is a movement toward more gender equity than noted in previous reports or often publicly appreciated. At the same time, the findings show that we are not there yet. The gap between female graduates and the pool of female applicants is very real, and suggests that focus next be placed on examining challenges such as family and child responsibilities, which typically impact women more than men."

*The study was sponsored by the National Science Foundation at the request of Congress. The National Academy of Sciences, National Academy of Engineering, Institute of Medicine, and National Research Council make up the National Academies. They are private, nonprofit institutions that provide science, technology, and health policy advice under a congressional charter. The Research Council is the principal operating agency of the National Academy of Sciences and the National Academy of Engineering. A committee roster follows.*

### **Be your best friend if you'll be mine: Penn's Alliance Hypothesis for Human Friendship**

PHILADELPHIA – University of Pennsylvania psychologists studying the cognitive mechanisms behind human friendship have determined that how you rank your best friends is closely related to how you think your friends rank you. The results are consistent with a new theory called the Alliance Hypothesis for Human Friendship, distinct from traditional explanations for human friendship that focused on wealth, popularity or similarity.

The study, performed by Penn cognitive psychologists Peter DeScioli and Robert Kurzban, has demonstrated that human friendship is caused, in part, by cognitive mechanisms aimed at creating a ready-made support group for potential conflicts. People call on friends for help in a variety of disputes, ranging from trivial arguments to violent fights. This study suggests that people have specialized decision processes that prioritize those individuals who tend to be most helpful in conflicts, those with fewer stronger commitments to others.

Researchers performed question-and-answer studies in which participants ranked their closest friends in a number of ways, including, for example, the benefits they receive from the friendship, the number of secrets shared and how long the friendship has been ongoing. Each time, whether participants were an online community, random passersby on a metropolitan street or undergraduate students in a laboratory, friendship rankings were most strongly correlated with individuals' own perceived rank among their partners' other friends.

"Historically, the main theory has been that humans build friendships in order to trade in goods and services," DeScioli, lead author, said. "The problem we focused on was that friendship involves more than exchange. People want friends who care about them and do not give just to get something back in return. We thought that theories about alliances might help explain why friends are primarily concerned with each others' needs rather than the benefits they can get in return for helping."

Traditional evolutionary approaches to explain human friendship apply the Theory of Reciprocal Altruism: Friends function as exchange partners; however, a wealth of empirical evidence from social psychology is inconsistent with the theory. For example, in prior studies it was shown that people do not keep regular tabs on the benefits given and received in close relationships. Also, people seem to help friends even when they are unlikely to be capable of repayment. For cognitive psychologists, it is unclear what humans and their complex brains are up to in creating these relationships.

The new Penn theory has origins in models of alliance building between nations, which prepare for conflict in advance but may not expect anything in return immediately.

"Friendships are about alliances," Kurzban, an associate professor, said. "We live in a world where conflict can arise and allies must be in position beforehand. This new hypothesis takes into account how we value those alliances. In a way, one of the main predictors of friendship is the value of the alliance. The value of an ally, or

friend, drops with every additional alliance they must make, so the best alliance is one in which your ally ranks you above everyone else as well."

In short, the hypothesis is much more optimistic about the reasons for friendship than existing theories which point toward popularity, wealth and proximity as reasons for friendship.

"In this hypothesis," Kurzban said, "it's not what you can do for me, it's how much you like me. In this manner even the weakest nations, for example, or the least popular kid at the party with nary an alliance in the room is set up to be paired with someone looking for a friend."

More darkly, the new model also serves as an explanation for some petty human behaviors not explained by traditional friendship theories. For example, the Alliance Hypothesis explains why people are extremely concerned with comparisons to others in their social circle. It also explains how jealousies and aggression can erupt among groups of friends as alliances are shifted and maintained.

If the Alliance Hypothesis for Human Friendship is correct, then theories about alliances from game theory and international relations might help us better understand friendship. These theories suggest that people in conflict would benefit strategically from ranking their friends, hiding their friend-rankings and ranking friends according to their own position in partners' rankings. To employ these tactics in their friendships, people need to gather and store information about their friends' other friendships. That is, they have to readily understand the social world not only from their own perspective but also from the perspectives of their friends.

Although friendship is a core element of human social life, its evolved functions have been difficult to understand. Human friendship occurs among individuals who are neither relatives nor mates, so the function of this cooperative behavior is not as clear as when reproduction or genetic relatives are involved. Similar relationships have been observed in non-human species -- hyenas use partners to gain access to carcasses and male dolphins employ "wingmen" to attain females for mating — and considerable progress has been made in understanding these non-human relationships. But the functions of human friendship have been more elusive. *The study, appearing in the current issue of the online journal Public Library of Science One, was conducted by DeScioli and Kurzban of the Department of Psychology in the School of Arts and Sciences at Penn.*

### **NEJM study finds radiofrequency ablation can reverse Barrett's esophagus, reduce cancer risk**

#### ***A common result of prolonged gastroesophageal reflux disease, Barrett's esophagus is associated with increased risk for esophageal cancer***

NEW YORK (May 29, 2009) -- Patients who have gastroesophageal reflux disease (GERD) for a prolonged period have an increased risk of developing Barrett's esophagus, a pre-cancerous condition where the tissue lining the esophagus becomes damaged by stomach acid and transformed into something like the inside of the stomach. New research finds that radiofrequency ablation -- an endoscopic procedure involving targeted thermal energy -- was very successful at restoring the esophagus and reducing risk for cancer.

The study was conducted at 19 centers nationally, including New York-Presbyterian Hospital/Columbia University Medical Center. Results are published in the May 28 New England Journal of Medicine along with an accompanying editorial, which hails it as a "landmark study in the field."

"The current standard of care for Barrett's esophagus has been watchful waiting or surveillance -- delaying surgery until the first sign of cancer. This study offers powerful evidence that treatment using radiofrequency ablation can help prevent esophageal cancer by completely reversing overall Barrett's esophagus and its more severe tissue changes, or dysplasias," says study senior author Dr. Charles Lightdale, a gastroenterologist at New York-Presbyterian Hospital/Columbia University Medical Center and professor of clinical medicine at Columbia University College of Physicians and Surgeons.

While it is still rare for Barrett's esophagus to develop into esophageal cancer, incidence of the cancer has increased fivefold over the last 30 years. Treating esophageal cancer involves major surgery to remove a section of the organ. Five-year survival is less than 15 percent.

In the study, 127 patients with Barrett's esophagus and dysplasia were randomized to receive either radiofrequency ablation (RFA) or a control group which received a non-therapeutic endoscopic surveillance procedure and followed over 12 months. Overall, only 1 percent of those receiving RFA developed cancer, compared with 9 percent in the control group, and 77.4 percent of RFA patients had complete eradication of the disease, compared with 2.3 percent in the control group.

For patients with small amounts of tissue change (dysplasia), a complete eradication of dysplasia occurred in 90.5 percent of those in the ablation group, compared with 22.7 percent in the control group. For patients with more advanced, "high grade" dysplasia, complete eradication occurred in 81.0 percent in the ablation group, compared with 19 percent in the control group.



Currently many patients with high-grade dysplasia undergo an esophagectomy, a major surgery that removes a section of the esophagus. "This study shows that minimally invasive RFA should be the standard of care for these patients," says Dr. Lightdale, who has offered the procedure to patients at New York-Presbyterian/Columbia over the last five years.

The study found side effects of RFA were mild, and included increased risk for chest pain and a narrowing (stricture) of the esophagus. There was one reported case of upper gastrointestinal hemorrhage.

"While our study didn't look at other interventions, it's notable that the side effects associated with radiofrequency ablation were significantly less than those reported in studies of photodynamic therapy, a laser-based approach," says Dr. Lightdale.

RFA for Barrett's esophagus is a half-hour outpatient procedure performed under mild sedation. The energy is highly controlled, and can be limited to the thin layer of the esophagus, preventing injury to healthy tissue. RFA technology is widely used to treat tumors in the liver, kidney and bones; used to restore normal heart rhythms; and for varicose veins.

Barrett's esophagus affects about 1 percent of adults in the United States. Men develop Barrett's esophagus twice as often as women. Approximately 10 percent of patients with chronic reflux have the condition. Half of Barrett's patients don't have heartburn.

"Advanced Barrett's esophagus diminishes the painful symptoms of acid reflux making its diagnosis difficult in many patients. Therefore, it's important for anyone who has had prolonged GERD to be screened," says Dr. Lightdale.

Now that radiofrequency ablation has been shown to be effective in patients with dysplastic Barrett's esophagus, the next step is to see if it works for patients with less severe disease.

*The study's lead author is Dr. Nicholas J. Shaheen of the University of North Carolina at Chapel Hill. The research was sponsored by BARRX Medical Inc., maker of the radiofrequency ablation equipment used in the study. For more information, patients may call (866) NYP-NEWS.*

## **Methanol challenges hydrogen to be fuel of the future**

**18:03 02 June 2009 by Colin Barras**

For years many companies, governments and researchers have predicted that our energy future must lie with the universe's simplest element. The mooted hydrogen economy would use the gas to store and transport renewable or low-carbon energy, and power fuel cells in the transport sector or in portable electronics.

But creating the necessary society-wide infrastructure has proved difficult and expensive to get off the ground. And now a rival idea, first suggested in 2006 by Nobel chemistry laureate George Olah at the University of Southern California, has received a boost. The methanol economy, say its supporters, could be with us much sooner than the hydrogen one.

### **Hydrogen dangers**

Olah's rationale is that modifying our existing oil and petrol-focused infrastructure to run on methanol will be much easier than refitting the world's liquid-fuel-based economy to deal with an explosive gas.

Methanol has already been used to power portable gadgets and could potentially power vehicles and other devices. Now US chemists have worked out the conditions needed to make the feedstock for methanol production using renewable energy.

The research is significant because just as the lack of an efficient way to generate and store hydrogen is a major barrier to the idea of running civilisation on it, sourcing methanol on a vast scale is a similarly major hurdle.

### **Clean solution**

The best way to make methanol is by steam reforming methane, produced when syngas - a mixture of hydrogen and carbon monoxide - is turned into liquid hydrocarbons via reactions such as the Fischer-Tropsch process.

The process is used today to make diesel and other liquid fuels from coal, and kept South African cars going during the country's international isolation in the 1980s and 90s.

However, the whole point of the methanol economy would be to create a greener society, so any syngas must come from an environmentally friendly source, not fossil fuels.

Now chemist Scott Barnett at Northwestern University in Evanston, Illinois, and colleagues have shown that a solid oxide electrolysis cell, more normally used to split water into hydrogen and oxygen, could be that source.

### **Viable brew**

Using a mix of one part CO<sub>2</sub>, one part hydrogen and two parts water in the device generates syngas at a rate which compares favourably with the processes used to make it from natural gas, says Barnett. At peak conditions of 800 °C and 1.3 volts, the system can produce 7 standard cubic centimetres of syngas per minute for every square centimetre of the electrolysis cell's surface.

The next stage, turning the syngas into methanol, is a standard industrial reaction that is well understood. Barnett's method requires a steady stream of water vapour and CO<sub>2</sub>, but both gases are released when the methanol is used in fuel cells, and could be captured and re-used, he says.

That would add to the costs involved, but a hydrogen economy would require similar gas-capture technology, says Barnett, because hydrogen production requires a plentiful source of fresh water, which is heavy to cart about.

Olah thinks Barnett's study is a useful one. "This [methanol economy] approach is now starting to be implemented around the world," he says. "New methanol plants are being built in China, South Korea, Japan and Iceland."

### **Limited scope**

But others remain sceptical that methanol will ever occupy more than a small niche. There are several well-known problems with the use of methanol. Like hydrogen, and unlike petrol, methanol is not a source of energy, but simply an energy store, points out Ulf Bossel at the European Fuel Cell Forum in Oberrohrdorf, Switzerland. "The energy carried by methanol is less than was needed to make it," he adds.

Barnett agrees that methanol is a poor substitute for using the power from a renewable generator like a wind turbine directly. But he says that in cases where direct use is not possible, liquid methanol beats the efficiency of hydrogen for storage and transportation.

Methanol could be used to store energy from renewable sources that often produce more electricity than is needed at a particular time, he says, and could also be useful at off-grid sites.

In these situations, Bossel agrees a modest methanol economy makes sense. "The hydrogen idea is gradually fading," he says. "Methanol could be a better solution because it is easier to handle."

*Journal reference: Energy and Fuels (DOI: 10.1021/ef900111f)*

### **Memory with a twist: NIST develops a flexible memristor**

Electronic memory chips may soon gain the ability to bend and twist as a result of work by engineers at the National Institute of Standards and Technology (NIST). As reported in the July 2009 issue of *IEEE Electron Device Letters*,\* the engineers have found a way to build a flexible memory component out of inexpensive, readily available materials.

Though not yet ready for the marketplace, the new device is promising not only because of its potential applications in medicine and other fields, but because it also appears to possess the characteristics of a memristor, a fundamentally new component for electronic circuits that industry scientists developed in 2008.\*\* NIST has filed for a patent on the flexible memory device (application #12/341.059).

Electronic components that can flex without breaking are coveted by portable device manufacturers for many reasons—and not just because people have a tendency to drop their mp3 players. Small medical sensors that can be worn on the skin to monitor vital signs such as heart rate or blood sugar could benefit patients with conditions that require constant maintenance, for example. Though some flexible components exist, creating flexible memory has been a technical barrier, according to NIST researchers.

Hunting for a solution, the researchers took polymer sheets—the sort that transparencies for overhead projectors are made from—and experimented with depositing a thin film of titanium dioxide, an ingredient in sunscreen, on their surfaces. Instead of using expensive equipment to deposit the titanium dioxide as is traditionally done, the material was deposited by a sol gel process, which consists of spinning the material in liquid form and letting it set, like making gelatin. By adding electrical contacts, the team created a flexible memory switch that operates on less than 10 volts, maintains its memory when power is lost, and still functions after being flexed more than 4,000 times.

What's more, the switch's performance bears a strong resemblance to that of a memristor, a component theorized in 1971 as a fourth fundamental circuit element (along with the capacitor, resistor and inductor). A memristor is, in essence, a resistor that changes its resistance depending on the amount of current that is sent through it—and retains this resistance even after the power is turned off. Industrial scientists announced they had created a memristor last year, and the NIST component demonstrates similar electrical behavior, but is also flexible. Now that the team has successfully fabricated a memristor, NIST can begin to explore the metrology that may be necessary to study the device's unique electrical behavior.

"We wanted to make a flexible memory component that would advance the development and metrology of flexible electronics, while being economical enough for widespread use," says NIST researcher Nadine Gergel-Hackett. "Because the active component of our device can be fabricated from a liquid, there is the potential that in the future we can print the entire memory device as simply and inexpensively as we now print a slide on an overhead transparency."

\* N. Gergel-Hackett, B. Hamadani, B. Dunlap, J. Suehle, C. Richter, C. Hacker, D. Gundlach. A flexible solution-processed memristor. *IEEE Electron Device Letters*, Vol. 30, No. 7. Posted online the week of June 8, 2009.

\*\* D. B. Strukov, G. S. Snider, D. R. Stewart, and S. R. Williams. The missing memristor found. *Nature*, Vol. 453, May 1, 2008.

## **Mind**

### **Hold Your Head Up. A Blush Just Shows You Care.**

**By BENEDICT CAREY**

As if splitting a pair of pants, telling a transparent lie or mispronouncing the word “epitome” weren’t humiliation enough, nature has provided humans, especially the fair-skinned kind, with a built-in scarlet letter. Jane Austen heroines may pink endearingly at a subtle breach in manners; millions more glow like a lava lamp in what feels like a public disrobing: the face, suddenly buck-naked.

People who become severely anxious in social situations often swear that the blush itself is the source of their problems, not a symptom. Doctors may even perform surgery — severing a portion of the sympathetic nerve chain, which runs down the back — to take the red out.

Yet even this operation usually doesn’t short-circuit the system entirely, because a blush is far more than a stigmata of embarrassment. It is a crucial signal in social interactions — one that functions more often to smooth over betrayals and blunders than to amplify them.

In a series of recent studies, psychologists have found that reddening cheeks soften others’ judgments of bad or clumsy behavior, and help to strengthen social bonds rather than strain them. If nothing else, the new findings should take some of the personal sting out of the facial fire shower when it inevitably hits.

“We are this hypersocial species that settles conflicts and misunderstandings face to face, and we need a way to repair daily betrayals and transgressions quickly,” said Dacher Keltner, a psychologist at the University of California, Berkeley, and the author of “Born to Be Good: The Science of a Meaningful Life” (Norton, 2009). “A blush comes online in two or three seconds and says, ‘I care; I know I violated the social contract.’ ”

For decades, research on blushing was itself a kind of embarrassment. In 1872, in “The Expressions of the Emotions in Man and Animals,” Charles Darwin described blushing as “the most peculiar and most human of all expressions.” Other primates may redden during sex, but to Darwin the blush mainly reflected the human capacity for imagining others’ perceptions. The expression is so variable that later researchers thought it might reflect cultural or personal differences.

But the most fundamental dimension of a blush may be its effect on other people. In a study for the current issue of the journal *Emotion*, Dutch researchers had 66 participants read vignettes about people who were caught in some transgression, like cheating on a spouse, and after each one study a photograph of the offender. The participants saw the person wearing one of four expressions: neutral; neutral colored by a blush; shame (head down, gaze averted); or shame colored by a blush. On scales from 0 to 100, they rated how sympathetic and trustworthy they thought the person was.

A blush — a slight but not obvious coloring in the cheeks — significantly improved their judgment of the offender, whether the underlying expression was neutral or downcast.

The same pattern emerged in judgments of mishaps, like spilling coffee in a stranger’s lap. “You will certainly be judged after a mishap or transgression, but the main finding here is that a blush remediates others’ judgments,” said the lead author, Corine Dijk, a psychologist at the University of Amsterdam, in a phone interview. Her co-authors were Peter J. de Jong of the University of Groningen and Madelon L. Peters of Maastricht University.

In groups that tease their members, both to humble them and to include them, blushing appears to be both payoff and penalty. In a 2001 paper that contrasts teasing and bullying, an act of aggressive isolation, Dr. Keltner and colleagues from Berkeley discuss one experiment in which members of a fraternity at the University of Wisconsin came into his lab, four at a time, to tease one another, using barbed nicknames. Each group included two senior house members and two recent pledges.

The young men ripped each other with abandon, calling each other “little impotent,” “heifer fetcher” and “another drunk,” among many other names that cannot be printed. The researchers carefully recorded the interactions and measured how well individuals got along by the end. The newer members were all but strangers to the more senior ones when the study began.

“It was a subtle effect, but we found that the frequency of blushing predicted how well these guys were getting along at the end,” Dr. Keltner said. Blushing seemed to accelerate the formation of a possible friendship rather than delay it.

People tease each other in part to avoid confrontations, he added, and because a blush is both obvious and hard to fake, it signals that the blusher cares about the relationship. Happy couples tease each other skillfully

and continually; so do good friends. “Blushing is the fulcrum on which these interactions turn,” Dr. Keltner said. “And when it appears, hostility usually subsides.”

On first dates, or in truly hostile standoffs, the person who holds his or her ground despite a blush exhibits a kind of emotional courage without speaking a word or making a move.

None of which is to say that a blush is always helpful. In a recent paper, “In Praise of Blushing,” W. Ray Crozier, a professor of psychology at the University of East Anglia in Britain, concludes that it “can serve a useful social function; alternatively it can create a social predicament and be a source of shame or embarrassment for the blusher.” Anyone who has had to stand up to a bully and blushed badly knows that the expression can look like a toreador’s cape.

Still, people who struggle with social anxiety tend to see only the downside of their blush, said Jerilyn Ross, director of the Ross Center for Anxiety and Related Disorders in Washington and the author of “One Less Thing to Worry About” (Ballantine, 2009).

“If I were to explain to them that a blush can be endearing, they would only get angry and say I didn’t understand,” Dr. Ross said. “I would risk losing my relationship with them.”

In therapy, she continued, she tries to get such people to focus their attention on the conversation, on the interaction they’re having, rather than the warmth in their face — to say, “I blush when I’m anxious; what does that mean?”

If recent research is any guide, it means they care about what’s happening around them. And that can be a lot better, psychologists agree, than not caring.

### **Findings**

## **In That Tucked Tail, Real Pangs of Regret?**

**By JOHN TIERNEY**

If you own a dog, especially a dog that has anointed your favorite rug, you know that an animal is capable of apologizing. He can whimper and slouch and tuck his tail and look positively mortified — “I don’t know what possessed me.” But is he really feeling sorry?

Could any animal feel true pangs of regret? Scientists once scorned this notion as silly anthropomorphism, and I used to side with the skeptics who dismissed these displays of contrition as variations of crocodile tears. Animals seemed too in-the-moment, too busy chasing the next meal, to indulge in much self-recrimination. If old animals had a song, it would be “My Way.”



**Viktor Koen**

Yet as new reports keep appearing - moping coyotes, rueful monkeys, tigers that cover their eyes in remorse, chimpanzees that second-guess their choices - the more I wonder if animals do indulge in a little paw-wringing.

Your dog may not share Hamlet’s dithering melancholia, but he might have something in common with Woody Allen.

The latest data comes from brain scans of monkeys trying to win a large prize of juice by guessing where it was hidden. When the monkeys picked wrongly and were shown the location of the prize, the neurons in their brain clearly registered what might have been, according to the Duke University neurobiologists who recently reported the experiment in *Science*.

“This is the first evidence that monkeys, like people, have ‘would-have, could-have, should-have’ thoughts,” said Ben Hayden, one of the researchers. Another of the authors, Michael Platt, noted that the monkeys reacted to their losses by shifting their subsequent guesses, just like humans who respond to a missed opportunity by shifting strategy. “I can well imagine that regret would be highly advantageous evolutionarily, so long as one doesn’t obsess over it, as in depression,” Dr. Platt said. “A monkey lacking in regret might act like a psychopath or a simian Don Quixote.”

In earlier experiments, both chimpanzees and monkeys that traded tokens for cucumbers responded negatively once they saw that other animals were getting a tastier treat — grapes — for the same price. They made angry sounds and sometimes flung away the cucumbers or their tokens, reported Sarah Brosnan, a psychologist at Georgia State University.

“I think animals do experience regret, as defined as the recognition of a missed opportunity,” Dr. Brosnan said. “In the wild, these abilities may help them to recognize when they should forage in different areas or find a different cooperative partner who will share the spoils more equitably.”

No one knows, of course, exactly how this sense of regret affects an animal emotionally. When we see a dog slouching and bowing, we like to assume he’s suffering the way we do after a faux pas, but maybe he’s just sending a useful signal: I messed up.

“It’s possible that this kind of social signal in animals could have evolved without the conscious experience of regret,” said Sam Gosling, a psychologist at the University of Texas, Austin. “But it seems more plausible that there is some kind of conscious experience even if it’s not the same kind of thing that you or I feel.”

Marc Bekoff, a behavioral ecologist at the University of Colorado, says he’s convinced that animals feel emotional pain for their mistakes and missed opportunities. In “Wild Justice,” a new book he wrote with the philosopher Jessica Pierce, Dr. Bekoff reports on thousands of hours of observation of coyotes in the wild as well as free-running domesticated dogs.

When a coyote recoiled after being bitten too hard while playing, the offending coyote would promptly bow to acknowledge the mistake, Dr. Bekoff said. If a coyote was shunned for playing unfairly, he would slouch around with his ears slightly back, head cocked and tail down, tentatively approaching and then withdrawing from the other animals. Dr. Bekoff said the apologetic coyotes reminded him of the unpopular animals skulking at the perimeter of a dog park.

“These animals are not as emotionally sophisticated as humans, but they have to know what’s right and wrong because it’s the only way their social groups can work,” he said. “Regret is essential, especially in the wild. Humans are very forgiving to their pets, but if a coyote in the wild gets a reputation as a cheater, he’s ignored or ostracized, and he ends up leaving the group.” Once the coyote is on his own, Dr. Bekoff discovered, the coyote’s risk of dying young rises fourfold.

If our pets realize what soft touches we are, perhaps their regret is mostly just performance art to sucker us. But I like to think that some of the ruefulness is real, and that researchers will one day compile a list of the Top 10 Pet Regrets. (You can make nominations at TierneyLab, at [nytimes.com/tierneylab](http://nytimes.com/tierneylab).) At the very least, I’d like to see researchers tackle a few of the great unanswered questions:

When you’re playing fetch with a dog, how much regret does he suffer when he gives you back the ball? As much as when he ends the game by hanging on to the ball?

Do animal vandals feel any moral qualms? After seeing rugs, suitcases and furniture destroyed by my pets, I’m not convinced that evolution has endowed animals with any reliable sense of property rights. But I’m heartened by Eugene Linden’s stories of contrite vandals in his book on animal behavior, “The Parrot’s Lament.”

He tells of a young tiger that, after tearing up all the newly planted trees at a California animal park, covered his eyes with his paws when the zookeeper arrived. And there were the female chimpanzees at the Tulsa Zoo that took advantage of a renovation project to steal the painters’ supplies, don gloves and paint their babies solid white. When confronted by their furious keeper, the mothers scurried away, then returned with peace offerings and paint-free babies.

How awkward is the King Kong Syndrome? Both male and female gorillas have become so fond of their human keepers that they’ve made sexual overtures — one even took to dragging his keeper by her hair. After the inevitable rebuff, do they regret ruining a beautiful friendship?

Do pet cats ever regret anything?

### **Sleeping with the enemy**

It has been linked to learning impairment, stroke and premature death. Now UNSW research has found that snoring associated with sleep apnoea may impair brain function more than previously thought.

Sufferers of obstructive sleep apnoea experience similar changes in brain biochemistry as people who have had a severe stroke or who are dying, the research shows.

A study by UNSW Brain Sciences, published this month in the *Journal of Cerebral Blood Flow and Metabolism*, is the first to analyse - in a second-by-second timeframe - what is happening in the brains of sufferers as they sleep. Previous studies have focused on recreating oxygen impairment in awake patients.

“It used to be thought that apnoeic snoring had absolutely no acute effects on brain function but this is plainly not true,” said lead author of the study, New South Global Professor Caroline Rae. Sleep apnoea affects as many as one in four middle-aged men, with around three percent going on to experience a severe form of the condition characterised by extended pauses in breathing, repetitive asphyxia and sleep fragmentation. Children with enlarged tonsils and adenoids are also affected, raising concerns of long-term cognitive damage.

Professor Rae and collaborators from Sydney University’s Woolcock Institute used magnetic resonance spectroscopy to study the brains of 13 men with severe, untreated, obstructive sleep apnoea. They found that even a moderate degree of oxygen desaturation during the patients’ sleep had significant effects on the brain’s bioenergetic status.

“The findings show that lack of oxygen while asleep may be far more detrimental than when awake, possibly because the normal compensatory mechanisms don’t work as well when you are asleep,” Professor Rae, who is based at the Prince of Wales Medical Research Institute, said.

“This is happening in someone with sleep apnoea acutely and continually when they are asleep. It’s a completely different biochemical mechanism from anything we’ve seen before and is similar to what you see in somebody who has had a very severe stroke or is dying.”

The findings suggested societal perceptions of snoring needed to change, Professor Rae said. “People look at people snoring and think it’s funny. That has to stop.”

Professor Rae said it was still unclear why the body responded to oxygen depletion in this way. It could be a form of ischemic preconditioning at work, much like in heart attack sufferers whose initial attack makes them more protected from subsequent attacks.

“The brain could be basically resetting its bioenergetics to make itself more resistant to lack of oxygen,” Professor Rae said. “It may be a compensatory mechanism to keep you alive, we just don’t know, but even if it is it’s not likely to be doing you much good.”

### **Well**

## **Better Running Through Walking**

**By TARA PARKER-POPE**

I am more couch potato than runner. But not long ago, I decided to get myself into shape to run in the New York City Marathon, on Nov. 1, just 152 days from now. (Not that I’m counting.)

To train for my first marathon, I’m using the “run-walk” method, popularized by the distance coach Jeff Galloway, a member of the 1972 Olympic team.

When I mentioned this to a colleague who runs, she snickered — a common reaction among purists.

But after interviewing several people who have used the method, I’m convinced that those of us run-walking the marathon will have the last laugh.

Contrary to what you might think, the technique doesn’t mean walking when you’re tired; it means taking brief walk breaks when you’re not.

Depending on one’s fitness level, a walk-break runner might run for a minute and walk for a minute, whether on a 5-mile training run or the 26.2-mile course on race day. A more experienced runner might incorporate a one-minute walk break for every mile of running.

Taking these breaks makes marathon training less grueling and reduces the risk of injury, Mr. Galloway says, because it gives the muscles regular recovery time during a long run. Walk breaks are a way for older, less fit and overweight people to take part in a sport that would otherwise be off limits. But most surprising are the stories from veteran runners who say run-walk training has helped them post faster race times than ever.

One of them is Tim Deegan of Jacksonville, Fla., who had run 25 marathons when his wife, Donna Deegan, a popular local newscaster and cancer survivor, began organizing a marathon to raise money for breast cancer research. When Mr. Galloway volunteered to help with the race, Ms. Deegan asked her husband to take part in run-walk training to show support. “The only reason I did this is because I love my wife,” said Mr. Deegan, 49. “To say I was a skeptic is to put it very nicely.”

But to his surprise, he began to enjoy running more, and he found that his body recovered more quickly from long runs. His times had been slowing — to about 3 hours 45 minutes, 15 minutes shy of qualifying for the Boston Marathon - but as he ran-walked his way through the Jacksonville Marathon, “I started thinking I might have a chance to qualify for Boston again.” He did, posting a time of 3:28.

Nadine Rihani of Nashville ran her first marathon at age 61, taking walk breaks. Her running friends urged her to adopt more traditional training, and she was eventually sidelined by back and hip pain. So she resumed run-walk training, and in April, at age 70, she finished first in her age group in the Country Music Marathon, coming in at 6:05. “My friends who were ‘serious’ runners said, ‘You don’t need to do those walk breaks,’ ” she said. “I found out the hard way I really did.”

Dave Desposato, a 46-year-old financial analyst, began run-walk training several years ago after excessive running resulted in an overuse injury. He finished this year’s Bayshore Marathon in Traverse City, Mich., in 3:31:42, cutting 12 minutes off his previous best.

“I run enough marathons now to see everybody totally collapsing at the end is very, very common,” he said. “You wish you could share your experience with them, but they have to be willing to listen first.”

Another unconventional element of walk-break training is the frequency - typically just three days a week, with two easy runs of 20 to 60 minutes each and a long run on the weekend. The walk breaks allow runners to build up their mileage without subjecting their bodies to the stress of daily running, Mr. Galloway said.



Many runners take their own version of walk breaks without thinking about it, he says: they slow down at water stations or reduce their pace when they tire. Scheduling walk breaks earlier in a run gives the athlete control over the race and a chance to finish stronger.

While I'm planning to use run-walk training to complete my first marathon, I've heard from many runners who adhere to a variety of training methods. So later this week, the Well blog will have a new feature: the Run Well marathon training tool, with which you can choose any of several coaches' training plans and then track your progress.

Besides Mr. Galloway, plans are being offered by the marathoner Greg McMillan, who is renowned for his detailed training plans that help runners reach their time goals; the New York Flyers, the city's largest running club, which incorporates local road races into its training; and Team for Kids, a New York Road Runners Foundation charity program that trains 5,000 adult runners around the world.

The Run Well series also gives you access to top running experts, advice from elite runners, reviews of running gadgets and regular doses of inspiration to get you race-ready.

So please join me, the coaches and other running enthusiasts every day at the Well blog, [nytimes.com/well](http://nytimes.com/well), during the next five months of training. For me, this is finally the year I'll run a marathon. I hope it will be your year too.

### **Women may not be so picky after all about choosing a mate**

EVANSTON, Ill. --- Men and women may not be from two different planets after all when it comes to choosiness in mate selection, according to new research from Northwestern University.

When women were assigned to the traditionally male role of approaching potential romantic partners, they were not any pickier than men in choosing that special someone to date, according to the speed dating study.

That finding, of course, is contrary to well established evolutionary explanations about mate selection. An abundance of such research suggests that women are influenced by higher reproductive costs (bearing and raising children) than men and thus are much choosier when it comes to love interests.

The new study is the latest research of two Northwestern psychologists whose well-reported work on speed dating offers unparalleled opportunities for studying romantic attraction in action.

Deviating from standard speed-dating experiments – and from the typical conventions at professional speed-dating events - women in the study were required to go from man to man during their four-minute speed dates half the time, rather than always staying put. In most speed-dating events, the women stay in one place as the men circulate.

"The mere act of physically approaching a potential partner, versus being approached, seemed to increase desire for that partner," said Eli Finkel, associate professor of psychology in the Weinberg College of Arts and Sciences at Northwestern and co-investigator of the study.

Regardless of gender, those who rotated experienced greater romantic desire for their partners, compared to those who sat throughout the event. The rotators, compared to the sitters, tended to have a greater interest in seeing their speed-dating partners again.

"Given that men generally are expected -- and sometimes required -- to approach a potential love interest, the implications are intriguing," Finkel said.

"Let's face it, even today, there is a huge difference in terms of who is expected to walk across the bar to say 'hi,'" added Northwestern's Paul Eastwick, the study's other co-investigator.

The study is forthcoming in *Psychological Science*, a journal of the Association for Psychological Science.

Three hundred fifty undergraduates were recruited for the study's speed-dating events. In half of the events, the men rotated while the women sat. In the remaining events, the women rotated. Following each four-minute "date," the participants indicated their romantic desire in that partner and how self-confident they felt. Following the event, the students indicated on a Website whether they would or would not be interested in seeing each partner again.

When the men rotated, the results supported the long-held notion of men being less selective. When the women rotated, this robust sex difference disappeared.

The study draws upon embodiment research that suggests that physical actions alter perception. In one such study, for example, participants who were told to pull an unrelated object toward themselves while evaluating Chinese ideographs rated them as prettier than participants who pushed an unrelated object away from themselves while viewing the symbols.

"The embodiment research shows that our physical activity and psychological processes interface in ways that are outside our conscious awareness," Finkel said. "In conjunction with this previous embodiment research, our speed-dating results strongly suggest that the mere act of approaching a potential love interest can boost desire."

The researchers suggest that confidence also may have affected the results. Approaching a potential date increases confidence, which in turn makes the approacher less selective.

The study presents a clear example of how inconspicuous gender norms (having men rotate and women sit) can not only affect the outcome of a study, but also skew the chances of a speed dater walking away with a potential match.

"Our society is structured in gendered ways that can be subtle but very powerful," Eastwick concluded. The study has implications both for companies that capitalize on the business of dating and for researchers concerned with how social norms may affect research.

### **Health workers may flee in pandemic panic**

\* 03 June 2009 by Rachel Nowak

HEALTHCARE workers will desert their posts in droves in a pandemic, unless the safety and psychological issues they face are addressed. So say surveys of doctors, nurses and other staff, such as lab techs, secretaries and porters, from around the world.

The worst predictions are for the UK, where as few as 15 per cent of workers would show up in a pandemic (BMC Public Health, DOI: 10.1186/1471-2458-9-142).

Elsewhere, the figures are better but still worrying. Two Australian surveys suggest that 60 to 80 per cent of workers would go to work (BMC Health Services Research, DOI: 10.1186/1472-6963-9-30; The Medical Journal of Australia, vol 187, p 676). Studies in Hong Kong and the US predict an 85 and 50 per cent turnout respectively.

Existing pandemic plans tend to focus on making sure workers are able to work, by providing transport or training for new roles. But "our study found that willingness to work is the most important factor in absenteeism", says Sarah Damery of the University of Birmingham, UK.

The surveys identify factors likely to increase someone's willingness to work. One is feeling valued, which could be especially important for ancillary staff, who are both most likely to say they wouldn't work and least likely to feel that their role is essential, says George Everly of the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland, who carried out a US survey (BMC Public Health, DOI: 10.1186/1471-2458-6-99). "You need to build a sense of identity and cohesion."

But for all healthcare workers, even those not in contact with sick patients, the biggest factor was their safety and that of their families. "Vaccination for workers and their families, and to some extent personal protective equipment, would potentially have a massive effect on absenteeism," says Damery.

In a pandemic, clinical staff would take priority in getting vaccines and drugs, but their families probably wouldn't, says Raina MacIntyre, an infectious disease expert at the University of New South Wales in Sydney, Australia. Instead, staff could be offered board away from home.

Offering more money to ancillary staff would do little to encourage them to work, says Charlene Irvin of St John Hospital and Medical Center in Detroit, Michigan.

### **Single women gaze longer**

#### ***Neuroscientists found woman's partner status relevant for her interest in the opposite sex***

A study by neuroscientist Heather Rupp and her team found that a woman's partner status influenced her interest in the opposite sex. In the study<sup>1</sup>, published in the March issue of Human Nature, women both with and without sexual partners showed little difference in their subjective ratings of photos of men when considering such measures as masculinity and attractiveness. However, the women who did not have sexual partners spent more time evaluating photos of men, demonstrating a greater interest in the photos. No such difference was found between men who had sexual partners and those who did not.

"These findings may reflect sex differences in reproductive strategies that may act early in the cognitive processing of potential partners and contribute to sex differences in sexual attraction and behavior," said Rupp, assistant scientist at The Kinsey Institute for Research in Sex, Gender and Reproduction at Indiana University in the US.

For the study, 59 men and 56 women rated 510 photos of opposite-sex faces for realism, masculinity/femininity, attractiveness, or affect. Participants were instructed to give their "gut" reaction and to rate the pictures as quickly as possible. The men and women ranged in age from 17 to 26, were heterosexual, from a variety of ethnic backgrounds and were not using hormonal contraception. Of the women, 21 reported they had a current sexual partner; 25 of the men reported having a sexual partner. This is the first study to report whether having a current sexual partner influences interest in the opposite sex. Other studies have demonstrated that hormones, relationship goals and social context influence such interest.

"That there were no detectable effects of sexual partner status on women's subjective ratings of male faces, but there were on response times, which emphasizes the subtlety of this effect and introduces the possibility that



sexual partner status impacts women's cognitive processing of novel male faces but not necessarily their conscious subjective appraisal," the authors wrote in the journal article. The researchers also note that influence of partner status in women could reflect that women, on average, are relatively committed in their romantic relationships, "which possibly suppresses their attention to and appraisal of alternative partners."

**Reference** <sup>1</sup>Rupp H et al. 2009. Partner Status Influences Women's Interest in the Opposite Sex. *Human Nature* DOI 10.1007/s12110-009-9056-6

### **Simple drug treatment may prevent nicotine-induced SIDS: Study**

A new study has identified a specific class of pharmaceutical drugs that could be effective in treating babies vulnerable to Sudden Infant Death Syndrome (SIDS), because their mothers smoked during pregnancy.

According to researchers at McMaster University, exposure of the fetus to nicotine results in the inability to respond to decreases in oxygen - known as hypoxia - which may result in a higher incidence of SIDS. In the same study on rats, they found that the diabetic medication 'glibenclamide' can reverse the effects of nicotine exposure, increasing the newborn's ability to respond to hypoxia and likely reducing the incidence of SIDS.

The findings are published today in the *Journal of Neuroscience*.

"During birth the baby rapidly changes its physiology and anatomy so that it can breathe on its own," explains Josef Buttigieg, lead author who conducted his research as a PhD graduate student in the department of Biology. "The stress of being born induces the release of the hormones adrenaline and noradrenaline - collectively called catecholamines - from the adrenal glands. During birth, these hormones in turn signal the baby's lungs to become ready for air breathing."

For some months after birth, the adrenal glands act as a critical oxygen sensor. A drop in blood oxygen levels will stimulate the release of catecholamines, which in turn signals the baby to take a deep breath, when an infant rolls on its face or has an irregular breathing pattern during sleep, for example. However, the ability to release those hormones during moments of apnea or asphyxia is impaired due to nicotine exposure.

During those episodes, specific proteins sensitive to hypoxia stimulate the cell to release catecholamines. A secondary class of proteins then acts as a 'brake', ensuring the cells do not over excite themselves during this stressful time. However, exposure of the fetus to nicotine results in higher levels of this brake protein.

"The result is like trying to drive your car with the parking brake on. You might go a little bit, but the brakes hold you back," explains Buttigieg. "In this case, the adrenal glands do not release catecholamines during hypoxia - for example during birth or a self-asphyxiation episode - often resulting in death."

But when researchers administered the drug glibenclamide in laboratory rats, which override the brake protein, the adrenal glands were able to respond to oxygen deprivation, therefore reversing the lethality of hypoxia.

"Our initial goal was really to understand how the nervous system regulates oxygen sensitivity of cells in the adrenal gland at a basic research level," says Colin Nurse, academic advisor on the study and a professor in the department of Biology. "We speculated that chemicals released from nerves might interact with adrenal cells and cause them to lose oxygen sensitivity. It turns out that nicotine mimics the effects of one of these chemicals, thereby allowing us to test the idea. The present study was significant in that it led to a mechanistic understanding of how nicotine works in this context."

*The study was funded in part by the Heart & Stroke Foundation of Ontario, Canadian Institutes of Health Research and Focus on Stroke.*

### **People who wear rose-coloured glasses see more**

June 2/09 **By Kim Luke**

A University of Toronto study provides the first direct evidence that our mood literally changes the way our visual system filters our perceptual experience suggesting that seeing the world through rose-coloured glasses is more biological reality than metaphor.

"Good and bad moods literally change the way our visual cortex operates and how we see," says Adam Anderson, a U of T professor of psychology. "Specifically our study shows that when in a positive mood, our visual cortex takes in more information, while negative moods result in tunnel vision. The study appears tomorrow in the *Journal of Neuroscience*.

The U of T team used functional magnetic resonance imaging to examine how our visual cortex processes sensory information when in good, bad, and neutral moods. They found that donning the rose-coloured glasses of a good mood is less about the colour and more about the expansiveness of the view.

The researchers first showed subjects a series of images designed to generate a good, bad or neutral mood. Subjects were then shown a composite image, featuring a face in the centre, surrounded by "place" images, such as a house. To focus their attention on the central image, subjects were asked to identify the gender of the person's face. When in a bad mood, the subjects did not process the images of places in the surrounding background. However, when viewing the same images in a good mood, they actually took in more information

— they saw the central image of the face as well as the surrounding pictures of houses. The discovery came from looking at specific parts of the brain - the parahippocampal “place area” - that are known to process places and how this area relates to primary visual cortical responses, the first part of the cortex related to vision. Images from the experiment are at the Affect & Cognition Lab website.

“Under positive moods, people may process a greater number of objects in their environment, which sounds like a good thing, but it also can result in distraction,” says Taylor Schmitz, a graduate student of Anderson’s and lead author of the study. “Good moods enhance the literal size of the window through which we see the world. The upside of this is that we can see things from a more global, or integrative perspective. The downside is that this can lead to distraction on critical tasks that require narrow focus, such as operating dangerous machinery or airport screening of passenger baggage. Bad moods, on the other hand, may keep us more narrowly focused, preventing us from integrating information outside of our direct attentional focus.”  
*The research is supported by the Canadian Institutes of Health Research and the Canada Research Chairs program.*

### **Hospitalized patients need better understanding of CPR and outcomes**

Many hospitalized patients overestimate their chance of surviving an in-hospital cardiac arrest and do not know what CPR really involves, a University of Iowa study has shown.

The study further showed that this lack of understanding of cardiopulmonary resuscitation may affect a patient's choice about whether to have orders in place to be resuscitated if they are dying.

The study, which also involved researchers in the Iowa City Veterans Affairs Medical Center, appeared in the June 1 issue of the Journal of Medical Ethics.

"The investigation indicates that doctors need to do more to help patients understand CPR procedures and 'do not resuscitate', or DNR, orders to avoid gaps between treatments used and patients' actual preferences," said the study's lead author Lauris Kaldjian, M.D., Ph.D., associate professor of internal medicine at the UI Roy J. and Lucille A. Carver College of Medicine and a physician with UI Hospital and Clinics.

"Our study showed that after people were asked about their goals of care and then informed about the chances of survival and good brain function after CPR, nearly one in five said their preferences about CPR had changed," added Kaldjian, who also directs the college's Program in Bioethics and Humanities.

The study involved 135 adults who were interviewed within 48 hours of being admitted to the hospital for general medical treatment from June to August 2007. Many other studies on resuscitation preferences have been based in outpatient settings or on hypothetical scenarios. In contrast, this study interviewed patients while they were being treated in the hospital, Kaldjian noted.

The patients' average age was 48 and just over half were women. Ethnicity was 92 percent white, 4 percent black, 3 percent Hispanic and 1 percent Asian. Very few patients had cancer or heart disease, but 61 percent of them had received intensive care in the past, indicating that they had already experienced serious illness.

The study showed that approximately three out of four patients thought they knew what CPR stood for and what it entails. However, only about 30 percent of patients actually knew that CPR stands for cardiopulmonary resuscitation. More important, only one in four patients (27 percent) understood that CPR in a hospital setting involves the use of an external defibrillator (electricity), and even fewer (7 percent) knew that dying patients would have a tube placed through the mouth and into the windpipe (intubation) and then be placed on a breathing machine. More than half of patients (59 percent) knew that manual chest compressions were used in CPR.

"CPR as it is used in the hospital setting is a more intensive procedure than many patients realized," Kaldjian said.

When patients were asked about the likelihood that CPR would allow them to survive and be discharged from hospital, the average prediction was 60 percent. The actual chance, on average, is about 18 percent.

When patients were additionally told that the odds of surviving CPR and still having good brain function are even lower -- only about 7 percent -- nearly one in five said that would influence them to change their preference regarding the use of resuscitation.

Kaldjian said that doctors should identify better ways to discuss resuscitation preferences with patients. "Placing these discussions in a wider context of goals of care may make it easier for patients to understand whether CPR is preferable, depending on the likelihood that CPR would help them achieve their care goals," he said.

"The hospital setting is often very busy, and it's hard to take time to talk about resuscitation preferences in a clear, informed and patient-centered way" he said. "We need to find feasible ways of having meaningful discussions, so that patients understand what doctors are telling them, and doctors understand what patients value and prefer."

*The investigation involved researchers with the Center for Research in the Implementation of Innovative Strategies in Practice at the Iowa City Veterans Affairs Medical Center.*

*The study was funded in part by a grant from the UI Carver College of Medicine to two research team members and by funding from the Veterans Administration National Quality Scholars Program to two additional team members.*

## **Scientists uncover mode of action of enzyme linked with several types of cancer**

### ***New study published in the journal Molecular Cell***

Scientists at the Institute for Research in Immunology and Cancer (IRIC) of the Université de Montréal have discovered a key mechanism used by cells to efficiently distribute chromosomes to new cells during cell multiplication. Published in the journal *Molecular Cell*, the study is the first to demonstrate that this mechanism relies on the polo kinase, an enzyme implicated in several cancers. Inhibiting this mechanism could be key to developing effective therapies to treat cancer.

Each human cell contains, in its nucleus, all the coding instructions necessary to direct the cell's activities. A complete set of those instructions is referred to as a genome. Cancer cells are capable of altering their genome in order to promote uncontrolled growth. "Cancer cells achieve this by gaining or losing specific chromosomes, or by inducing structural defects in their genome," explains Damien D'Amours, Principal Investigator at IRIC and director of the study, "We discovered that the polo kinase, overexpressed in a broad range of human tumours, tells the chromosomes exactly when to condense during cell division."

Misregulation of the polo kinase is associated with cancers, thereby suggesting a link between defects in chromosome condensation and the formation of tumours. "Pharmaceutical companies and independent researchers are already working on the development of new cancer drugs to inhibit the activity of the polo kinase," points out Damien D'Amours, "Understanding this enzyme's mode of action should enable us to control it. Such knowledge may reveal itself to be key in developing effective therapies to treat cancer."

In a preview article commissioned by *Molecular Cell*, world leader in chromosome dynamics Tatsuya Hirano, of the Riken Advanced Science Institute in Japan, qualifies the research as a tour de force study that will help address outstanding questions in the field.

## **Foreign accent syndrome doesn't mean brain damage**

**\* 14:03 03 June 2009 by Ewen Callaway**

A rare and mysterious syndrome that causes people to sound foreign has become even more baffling. Until now, the condition has been linked with damage in certain brain areas, but researchers have found two people with no trace of brain damage who have nevertheless sounded foreign since childhood.

This could prompt neurologists and linguists to rethink the origins of foreign accent syndrome (FAS) and may even point toward a genetic cause, says Peter Mariën, a neurologist at Middelheim General Hospital and the University of Antwerp, Belgium, who led the study. "There is no such thing as one simple recipe that explains what happens to a person who has foreign accent syndrome," he says.

Brain damage or developmental problems could occur in brain circuits responsible for the timing, tone and pronunciation of speech, causing accents to sound foreign.

"They know perfectly what to say," Mariën says. "They have the idea, they have the concept, but the organisation of the articulation patterns is disrupted."

### **Ear of the beholder**

People with FAS aren't reverting to a childhood accent or one they picked up from others, says Sheila Blumstein, a cognitive linguist at Brown University in Providence, Rhode Island, who was not involved in the study. They just sound foreign. "A lot of us have concluded that foreign accent syndrome is in the ears of the beholder," she says.

One person's Czech-sounding accent could remind another person of Russian and yet another of French. In fact, studies of FAS patients have shown that listeners show little agreement in assigning an accent to a particular language.

That was certainly true for the people that Mariën's team studied. Different listeners in a panel thought a 29-year-old woman known as TL sounded French, German, Scandinavian or Moroccan when she spoke her native Dutch. KL, a 7-year-old boy, sounded like a native Frenchman to most, but Moroccan, Asian or African to others.

Neither patient had a history of brain trauma, and, in the case of KL, magnetic-resonance brain imaging showed no abnormalities. This stands in stark contrast to most other people with FAS, who have lesions or damage in brain areas thought to be involved in speech and language.

"If it is a neural system, as we're sure it is, then it's certainly possible that even in developmental stages [FAS] might emerge," Blumstein says.

The possibility of a developmental origin for FAS suggests that genetic mutations could be associated with the syndrome. Mariën's team has begun working with a young woman with signs of FAS who says that her sister speaks similarly. "Can we identify, in these developmental cases, a genetic basis?" he wonders.  
*Journal reference: Cortex (vol 45, p 870)*

### Hybrid hearts could solve transplant shortage

\* 03 June 2009 by Andy Coghlan

"IT'S amazing, absolutely beautiful," says Doris Taylor, describing the latest addition to an array of tiny thumping hearts that sit in her lab, hooked up to an artificial blood supply.

The rat hearts beat just as if there were inside a live animal, but even more remarkable is how each one has been made: by coating the stripped-down "scaffolding" of one rat's heart with tissue grown from another rat's stem cells.

Taylor, a stem cell scientist at the University of Minnesota in Minneapolis, now wants to repeat the achievement on a much larger scale, by "decellularising" hearts, livers and other organs taken either from human cadavers or from larger animals such as pigs, and coating them in stem cells harvested from people.

This could lead to a virtually limitless supply of organs for transplantation that are every bit as intricate as those that grow naturally, except that they don't provoke the catastrophic immune response that obstructs the use of traditional "xenotransplants".



*A "decellularised" pig's heart*

The organs don't provoke the immune response that prevents traditional xenotransplants

"We're already working with heart, kidney, liver, lung, pancreas, gallbladder and muscle," Taylor says. Rival groups are using similar procedures to create new livers and muscle too.

Human organs for transplant are scarce. One option is to engineer organs from scratch in the lab, using artificial scaffolds. While bladders and skin can be grown in the lab, growing more complex organs and their intricate blood-vessel networks, has proved tricky.

Xenotransplants from pigs are another possibility, though fraught with problems. You have to prevent the recipient's immune system from destroying the organ, and also ensure the transplant is free of pig viruses that could be passed on.

Taylor's organs avoid these problems. For starters, building an intricate scaffold from scratch is unnecessary. "It's letting nature do most of the work," she says. What's more, because the stem cells that "clothe" the naked scaffold are taken from the patient, the organ stands a higher chance of being accepted by their immune system.

The idea is fairly simple: take an organ from a human donor or animal (see image), and use a mild detergent to strip away flesh, cells and DNA (see image) so that all is left is the inner "scaffold" of collagen, an "immunologically inert" protein (see image). Add stem cells from the relevant patient to this naked shell of an organ and they will differentiate into all the cells the organ needs to function without inducing an immune response after transplant, or any new infections.

The idea has already worked with simple organs. Last year Claudia Castillo received a transplant made a stripped-down windpipe from a dead human donor. Researchers cut it to size and seeded the scaffold with her stem cells, which grew into the right tissues and gave her a new windpipe. Anthony Hollander of the University of Bristol, UK, a member of the team, says Castillo no longer needs to take drugs and is back at her job.

Taylor's team is using the same technique to create much more complex organs such as hearts, and extending it to using animal, as well as human, scaffolds.

A big challenge with complex organs is ensuring that all their cells are infused with blood. Without blood, cells in the centre of the organ would be starved of oxygen and die after transplantation. Taylor says her method overcomes this problem.

A big breakthrough came in January 2008, when her team produced a beating heart by filling a rat heart scaffold with heart cells from newborn rats (*Nature Medicine*, vol 14, p 213). These hearts kept their 3D shape, including spaces for all the blood vessels. When they were seeded with new cells (see image), some grew into blood vessel lining (see image).

Since then, Taylor says they have managed to "pretty much repopulate the whole vascular tree" with cells, which includes veins, arteries and capillaries. "Because we've retained the blood vessels, we can take the plumbing and hook it up to the recipient's natural blood supply," says Taylor. "That's the beauty of this."

Although Taylor only added stem cells to the hearts, these cells differentiated into many different cells, in all the correct places, which is the best part of using decellularised scaffolds. The stem cells transformed into endothelial cells in the ventricles and atria, for example, and into vascular and smooth-muscle cells in the spaces for blood vessels, just as in a natural heart. Taylor thinks this happened because she pumped blood and nutrients through the organ, producing pressure in each zone which helps to determine how cells differentiate there.

But chemical, as well as mechanical, cues seem to have guided differentiation. Taylor has evidence that growth factors and peptides remained anchored to the scaffold even after the flesh was washed off. These chemicals likely signalled to the stem cells, indicating how many should migrate to which areas and what to change into in each zone. "Our mantra is to give nature the tools and get out of the way," she says.

Her team has implanted the reclothed hearts into the abdomens of rats, where they survived temporarily and were not rejected. The next step is to see if the transplants can replace an existing heart and keep the animal alive and healthy. To do this, Taylor says they will need to come up with ways to grow more muscle tissue on the hearts. "We've built the vasculature but we don't think we've built enough muscle to keep animals alive."

The next step is to see if the transplants can replace an existing heart and keep the rat alive and healthy.



*A rat heart undergoing decellularisation (top three images), and during recellularisation (bottom) (Image: courtesy of the University of Minnesota)*

She is also gearing up to repeat the rat experiments with pig hearts and livers. This could be easier because pig organs are larger and easier to handle than tiny rat hearts. Decellularised livers could also appear in humans before hearts because it may not be necessary to recreate entire livers for them to be useful.

Others are also working on livers. Steven Badylak says he has unpublished "proof of concept" that liver recellularisation works in rats and mice. A team lead by Martin Yarmush at Massachusetts General Hospital in Boston has manufactured recellularised rat grafts that provide liver function "in the lab and when transplanted", according to team member Korkut Uygun. But he stresses that the team's ultimate goal is to decellularise human, not animal, organs for transplantation.

Not everyone believes that turning decellularised tissue into a complex, functional organ is as simple as it sounds. "We're a long way from being able to make functional tissues and organs," says Alan Colman of the Singapore Stem Cell Consortium. "We'll be able to make structures that look like the organ, but with almost none of the correct functionality."

David Cooper of the University of Pittsburgh School of Medicine in Pennsylvania, a leading developer of xenotransplants, says that "naked" pig hearts would still carry traces of alpha-Gal, which the human immune system recognises and will attack.

But Chris Mason, professor of regenerative medicine at University College London points out that many decellularised pig components have been used in people without the need for immunosuppressive drugs (see "Pig parts"). He says sufficiently rigorous sterilisation destroys these residues. Otherwise, says Mason, millions of people would already have had adverse reactions to the pig heart valves and tissues they've received.

Taylor says people who find the idea of pig parts unacceptable should consider their current uses in humans. "We're not ready for prime time yet, but we're moving in the right direction," she says.

Pig parts already commonplace

**IMPLANTING** organs made from the scaffold of a pig organ may sound off-putting and even dangerous, but millions of patients have already been treated with decellularised pig parts without being infected by stowaway pig viruses or suffering disastrous immunological reactions.

Pig heart valves are often used to replace faulty ones in people. In the past, patients who got such valves had to take immunosuppressive drugs. But this isn't necessary with newer pig valves, made by the company AutoTissue in Berlin, which have been thoroughly decellularised.

For years, companies have also been selling decellularised pig gut to produce patches that help the healing of diabetic ulcers, hernias and strained ligaments. Cook Biotech of West Lafayette, Indianapolis, sells patches made from pig sub-mucosal collagen membrane, which provides mechanical strength to the small intestine.

"Since 1998, we've treated more than a million patients," says the company's Michael Hiles. Meanwhile, Tissue Regenix of Leeds, UK, is about to start testing tissue from pig heart membranes for patching up holes in arteries.

Chris Mason, professor of regenerative medicine at University College London, says the work of these companies bodes well for the idea of one day implanting much more complicated decellularised pig organs into people.

## Mammoths Roasted in Prehistoric Kitchen Pit

Jennifer Viegas, Discovery News

Central Europe's prehistoric people would likely have been amused by today's hand-sized hamburgers and hot dogs, since archaeologists have just uncovered a 29,000 B.C. well-equipped kitchen where roasted gigantic mammoth was one of the last meals served.

The site, called Pavlov VI in the Czech Republic near the Austrian and Slovak Republic borders, provides a homespun look at the rich culture of some of Europe's first anatomically modern humans.

While contemporaneous populations near this region seemed to prefer reindeer meat, the Gravettian residents of this living complex, described in the latest issue of the journal *Antiquity*, appeared to seek out more super-sized fare.



***One Big BBQ Archaeologists have uncovered a 29,000 B.C. well-equipped "kitchen" where roasted gigantic mammoth was one of the last meals served. Here, some remains of the prehistoric BBQ -- a mammoth bone -- is excavated. Jiri Svoboda and Antiquity [View a slide show of the prehistoric grill site here.](#)***

"It seems that, in contrast to other Upper Paleolithic societies in Moravia, these people depended heavily on mammoths," project leader Jiri Svoboda told Discovery News.

Svoboda, a professor at the University of Brno and director of its Institute of Archaeology, and colleagues recently excavated Pavlov VI, where they found the remains of a female mammoth and one mammoth calf near a 4-foot-wide roasting pit. Arctic fox, wolverine, bear and hare remains were also found, along with a few horse and reindeer bones.

The meats were cooked luau-style underground. Svoboda said, "We found the heating stones still within the pit and around."

Boiling pits existed near the middle roaster. He thinks "the whole situation -- central roasting pit and the circle of boiling pits -- was sheltered by a teepee or yurt-like structure."

It's unclear if seafood was added to create a surf-and-turf meal, but multiple decorated shells were unearthed. Many showed signs of cut marks, along with red and black coloration. The scientists additionally found numerous stone tools, such as spatulas, blades and saws, which they suggest were good for carving mammoths.

Perforated, decorative pebbles, ceramic pieces and fragments of fired clay were also excavated. The living unit's occupants left their fingerprints on some of the clay pieces, which they decorated with impressions made from reindeer hair and textiles.

Some items might have held "magical" or ritualistic significance, according to the scientists. One such artifact looks to be the head of a lion.

"This carnivore head was first modeled of wet clay, then an incision was made with a sharp tool, and finally the piece was heated in the fire, turned into some kind of ceramic," Svoboda explained.

"We hypothesize that this may be sympathetic magic."

"Sympathetic magic" often involves the use of effigies or fetishes, resembling individuals or objects, and is meant to affect the environment or the practitioners themselves.



***Lion Head This figure appears to represent the head and neck of a carnivore (probably a lion). Archaeologists say some of these kinds of items might have held magical or ritualistic significance to the ancient people. The carnivore head was first made from wet clay, then an incision was made with a sharp tool, and finally piece was heated in the fire and turned into ceramic.***

Archaeologist Erik Trinkaus of Washington University supports the new study, saying the site was "excavated meticulously" by Svoboda and his team.

"This is one more example, in this case from modern detailed excavation and analysis, of the incredibly rich human behavior from this time period," Trinkaus told Discovery News.

## Zimmermann et al.: 'Report: Reconstructing the evolution of laughter in great apes and humans'

Like human infants, young apes are known to hoot and holler when you tickle them. But is it fair to say that those playful calls are really laughter? The answer to that question is yes, say researchers reporting online on June 4th in *Current Biology*, a Cell Press publication.

"This study is the first phylogenetic test of the evolutionary continuity of a human emotional expression," said Marina Davila Ross of the University of Portsmouth in the United Kingdom. "It supports the idea that there is laughter in apes."

The researchers analyzed the recorded sounds of tickle-induced vocalizations produced by infant and juvenile orangutans, chimpanzees, gorillas, and bonobos, as well as those of human infants. A quantitative phylogenetic analysis of those acoustic data found that the best "tree" to represent the evolutionary relationships among those sounds matched the known evolutionary relationships among the five species based on genetics. The researchers said that the findings support a common evolutionary origin for the human and ape tickle-induced expressions.

They also show that laughter evolved gradually over the last 10 to 16 million years of primate evolutionary history. But human laughter is nonetheless acoustically distinct from that of great apes and reached that state through an evident exaggeration of pre-existing acoustic features after the hominin separation from ancestors shared with bonobos and chimps, about 4.5 to 6 million years ago, Davila Ross says. For instance, humans make laughter sounds on the exhale. While chimps do that too, they can also laugh with an alternating flow of air, both in and out. Humans also use more regular voicing in comparison to apes, meaning that the vocal cords regularly vibrate.

Davila Ross said they were surprised to find that gorillas and bonobos can sustain exhalations during vocalization that are three to four times longer than a normal breath cycle -- an ability that had been thought to be a uniquely human adaptation, important to our capacity to speak.

"Taken together," the researchers wrote, "the acoustic and phylogenetic results provide clear evidence of a common evolutionary origin for tickling-induced laughter in humans and tickling-induced vocalizations in great apes. While most pronounced acoustic differences were found between humans and great apes, interspecific differences in vocal acoustics nonetheless supported a quantitatively derived phylogenetic tree that coincides with the well-established, genetically based relationship among these species. At a minimum, one can conclude that it is appropriate to consider 'laughter' to be a cross-species phenomenon, and that it is therefore not anthropomorphic to use this term for tickling-induced vocalizations produced by the great apes."

*The researchers include Marina Davila Ross, University of Portsmouth, Portsmouth, UK, Institute of Zoology, University of Veterinary Medicine Hannover, Hannover, Germany; Michael J Owren, Georgia State University, Atlanta, GA; and Elke Zimmermann, Institute of Zoology, University of Veterinary Medicine Hannover, Hannover, Germany.*

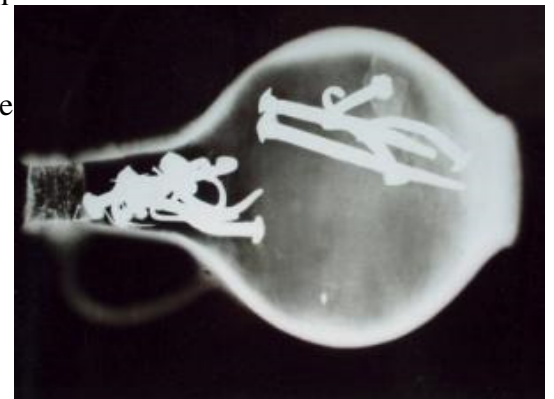
### London's magical history uncorked from 'witch bottle'

\* 00:01 04 June 2009 by Linda Geddes

A rare insight into the folk beliefs of 17th-century Britons has been gleaned from the analysis of a sealed "witch bottle" unearthed in Greenwich, London, in 2004. Witch bottles were commonly buried to ward off spells during the late 16th and 17th centuries, but it is very rare to find one still sealed.

"So many have been dug up and their contents washed away down the sink," says Alan Massey, a retired chemist formerly at the University of Loughborough, UK, who has examined so-called "magical" artifacts and was asked to analyse the contents of the bottle. "This is the first one that has been opened scientifically."

During the 17th century, British people often blamed witches for any ill health or misfortune they suffered, says Massey. "The idea of the witch bottle was to throw the spell back on the witch," he says. "The urine and the bulb of the bottle represented the waterworks of the witch, and the theory was that the nails and the bent pins would aggravate the witch when she passed water and torment her so badly that she would take the spell back off you."



*X-rays showing contents of the witch bottle found at Greenwich (Image: Alan Massey/R. J. Bostock)*

The salt-glazed jar was discovered 1.5 metres below ground by archaeologists from The Maritime Trust, a Greenwich-based charity that preserves historic sailing vessels. When it was shaken, the bottle splashed and rattled, and an X-ray showed pins and nails stuck in the neck, suggesting that it had been buried upside down.

Further computed tomography scans showed it to be half-filled with liquid, which later analysis showed to be human urine. The bottle also contained bent nails and pins, a nail-pierced leather "heart", fingernail clippings, navel fluff and hair. The presence of iron sulphide in the mixture also suggests that sulphur or brimstone had been added.

"Prior to this point, all we really knew about what was in witch bottles was what we read from documents from the 17th century," says Brian Hoggard, an independent expert on British witchcraft who helped analyse the bottle. These texts suggest "recipes" for filling a witch bottle, but don't tell us what actually went into them.

Sulphur is not mentioned in any recipe Massey has seen, although a previously discovered bottle seemed to contain the remains of some matches, he says. "If you think about where sulphur came from in those days, it spewed out of volcanic fumaroles from the underworld. It would have been the ideal thing to [kill] your witch, if you wished to."

Further analysis of the urine showed that it also contained cotinine, a metabolite of nicotine, suggesting that it came from a smoker, while the nail clippings appear quite manicured, suggesting that a person of some social standing created the bottle.

"It's confirming what 17th-century documents tell us about these bottles, how they were used and how you make them," says Owen Davies, a witchcraft expert at the University of Hertfordshire in Hatfield, UK. "The whole rationale for these bottles was sympathetic magic – so you put something intimate to the bewitched person in the bottle and then you put in bent pins and other unpleasant objects which are going to poison and cause great pain to the witch." *Journal reference: British Archaeology*

### **High population density triggers cultural explosions**

Increasing population density, rather than boosts in human brain power, appears to have catalysed the emergence of modern human behaviour, according to a new study by UCL (University College London) scientists published in the journal *Science*. High population density leads to greater exchange of ideas and skills and prevents the loss of new innovations. It is this skill maintenance, combined with a greater probability of useful innovations, that led to modern human behaviour appearing at different times in different parts of the world.

In the study, the UCL team found that complex skills learnt across generations can only be maintained when there is a critical level of interaction between people. Using computer simulations of social learning, they showed that high and low-skilled groups could coexist over long periods of time and that the degree of skill they maintained depended on local population density or the degree of migration between them. Using genetic estimates of population size in the past, the team went on to show that density was similar in sub-Saharan Africa, Europe and the Middle-East when modern behaviour first appeared in each of these regions. The paper also points to evidence that population density would have dropped for climatic reasons at the time when modern human behaviour temporarily disappeared in sub-Saharan Africa.

Adam Powell, AHRC Centre for the Evolution of Cultural Diversity, says: "Our paper proposes a new model for why modern human behaviour started at different times in different regions of the world, why it disappeared in some places before coming back, and why in all cases it occurred more than 100,000 years after modern humans first appeared.

"By modern human behaviour, we mean a radical jump in technological and cultural complexity, which makes our species unique. This includes symbolic behavior, such as abstract and realistic art, and body decoration using threaded shell beads, ochre or tattoo kits; musical instruments; bone, antler and ivory artefacts; stone blades; and more sophisticated hunting and trapping technology, like bows, boomerangs and nets.

Professor Stephen Shennan, UCL Institute of Archaeology, says: "Modern humans have been around for at least 160,000 to 200,000 years but there is no archaeological evidence of any technology beyond basic stone tools until around 90,000 years ago. In Europe and western Asia this advanced technology and behaviour explodes around 45,000 years ago when humans arrive there, but doesn't appear in eastern and southern Asia and Australia until much later, despite a human presence. In sub-Saharan Africa the situation is more complex. Many of the features of modern human behaviour – including the first abstract art – are found some 90,000 years ago but then seem to disappear around 65,000 years ago, before re-emerging some 40,000 years ago.

"Scientists have offered many suggestions as to why these cultural explosions occurred where and when they did, including new mutations leading to better brains, advances in language, and expansions into new environments that required new technologies to survive. The problem is that none of these explanations can fully account for the appearance of modern human behaviour at different times in different places, or its temporary disappearance in sub-Saharan Africa."

Dr Mark Thomas, UCL Genetics, Evolution and Environment, says: "When we think of how we came to be the sophisticated creatures we are, we often imagine some sudden critical change, a bit like when the black



monolith appears in the film 2001: A Space Odyssey. In reality, there is no evidence of a big change in our biological makeup when we started behaving in an intelligent way. Our model can explain this even if our mental capacities are the same today as they were when we first originated as a species some 200,000 years ago.

"Ironically, our finding that successful innovation depends less on how smart you are than how connected you are seems as relevant today as it was 90,000 years ago."

### **A new lead for autoimmune disease**

#### ***A small-molecule drug inhibits Th17 cells, eases symptoms in mouse model***

A drug derived from the hydrangea root, used for centuries in traditional Chinese medicine, shows promise in treating autoimmune disorders, report researchers from the Program in Cellular and Molecular Medicine and the Immune Disease Institute at Children's Hospital Boston (PCMM/IDI), along with the Harvard School of Dental Medicine. In the June 5 edition of *Science*, they show that a small-molecule compound known as halofuginone inhibits the development of Th17 cells, immune cells recently recognized as important players in autoimmune disease, without altering other kinds of T cells involved in normal immune function. They further demonstrate that halofuginone reduces disease pathology in a mouse model of autoimmunity.

Currently there is no good treatment for autoimmune disorders; the challenge has been suppressing inflammatory attacks by the immune system on body tissues without generally suppressing immune function (thereby increasing risk of infections). The main treatment is antibodies that neutralize cytokines, chemical messengers produced by T cells that regulate immune function and inflammatory responses. However, antibodies are expensive, must be given intravenously and don't address the root cause of disease, simply sopping up cytokines rather than stopping their production; patients must therefore receive frequent intravenous infusions to keep inflammation in check. Powerful immune-suppressing drugs are sometimes used as a last resort, but patients are left at risk for life-threatening infections and other serious side effects.

Through a series of experiments, the researchers show that halofuginone prevents the development of Th17 cells in both mice and humans, halts the disease process they trigger, and is selective in its effects. It also has the potential to be taken orally. "This is really the first description of a small molecule that interferes with autoimmune pathology but is not a general immune suppressant," says Mark Sundrud, PhD, of the PCMM/IDI, the study's first author.

Recognized only since 2006, Th17 cells have been implicated in a variety of autoimmune disorders including inflammatory bowel disease, rheumatoid arthritis, multiple sclerosis, type 1 diabetes, eczema and psoriasis. They are genetically distinct from the other major categories of T-cells (Th1, Th2 and T-regulatory cells).

Th17 cells normally differentiate from "naïve" CD4+ T cells, but when Sundrud and colleagues cultured mouse CD4+ T-cells along with cytokines that normally induce Th17 development, there was a pronounced decrease in Th17 cells – but not in Th1, Th2 or T regulatory cells – when halofuginone was added. Similarly, in cultured human CD4+ T-cells, halofuginone selectively suppressed production of IL-17, the principal cytokine made by Th17 cells.

And in mice with experimental autoimmune encephalitis (EAE), an artificially-induced immune disease resembling multiple sclerosis in humans, and marked by infiltration of Th17 cells into the central nervous system, low-dose halofuginone treatment significantly reduced both the development of EAE and its severity. (In mice with another form of EAE that doesn't involve Th17 cells, halofuginone had no effect.)

Wondering how halofuginone works, the researchers did microarray studies of the halofuginone-treated cells to examine patterns of gene expression in response to the drug. Unexpectedly, many genes involved in stress responses were turned on. Eventually, they found that halofuginone acts by activating a biochemical pathway known as the "amino acid starvation response," or AAR, which typically protects cells when amino acids, essential building blocks of proteins, are in short supply. When excess amino acids were added to cultured T-cells exposed to halofuginone, the AAR didn't switch on, and Th17 cells were able to develop. Conversely, the researchers were able to inhibit Th17 differentiation simply by depleting amino acids, thereby inducing the AAR.

Why would the AAR prevent Th17 cells from forming? The researchers propose that the AAR has an energy-saving function, slowing down a cell's building activities to conserve amino acids. "When a cell senses amino acid deprivation, it tries to conserve amino acids by preventing specific types of responses that are energetically expensive," says Sundrud. "In inflamed tissues, a lot of cells are producing a lot of protein, so it would make sense that a cell with amino acid deprivation would want to block signals that promote inflammation."

Halofuginone is one of the 50 fundamental herbs of traditional Chinese medicine, and has been used as an antimalarial agent. Decades ago, the U.S. Army tried to improve upon its antimalarial properties, without success. It has been in clinical trials for scleroderma, but because it is now in the public domain, the pharmaceutical industry has not shown interest in further developing it therapeutically.

But halofuginone, or some yet-to-be developed derivative compound, could potentially be used to address any autoimmune or inflammatory disease related to Th17 cells by activating the AAR, the researchers say.

"Remarkably, halofuginone evokes the AAR in all cells but selectively inhibits T-cell inflammatory responses," says Anjana Rao, PhD, of the PCMM/IDI, a senior investigator on the study. "This recalls the actions of cyclosporin A and FK506, two other immunosuppressive drugs that block the activity of calcineurin. Calcineurin is present in all cells, but selectively prevents the rejection of heart, lung, liver and bone marrow transplants when given to patients. These drugs revolutionized transplant medicine when they were introduced over 20 years ago, and halofuginone may herald a revolution in the treatment of certain types of autoimmune/inflammatory diseases."

*Malcolm Whitman, PhD and Tracy Keller, PhD, of the Harvard School of Dental Medicine, and Anjana Rao, PhD, of the PCMM/IDI, were the study's senior investigators. The study was funded by grants from the National Institutes of Health, the Juvenile Diabetes Research Foundation, and the Cancer Research Institute.*

### **New 'molecular clock' aids dating of human migration history**

Researchers at the University of Leeds have devised a more accurate method of dating ancient human migration – even when no corroborating archaeological evidence exists.

Estimating the chronology of population migrations throughout mankind's early history has always been problematic. The most widely used genetic method works back to find the last common ancestor of any particular set of lineages using samples of mitochondrial DNA (mtDNA), but this method has recently been shown to be unreliable, throwing 20 years of research into doubt.

The new method refines the mtDNA calculation by taking into account the process of natural selection – which researchers realised was skewing their results – and has been tested successfully against known colonisation dates confirmed by archaeological evidence, such as in Polynesia in the Pacific (approximately 3,000 years ago), and the Canary Islands (approximately 2,500 years ago).

Says PhD student Pedro Soares who devised the new method: "Natural selection's very gradual removal of harmful gene mutations in the mtDNA produces a time-dependent effect on how many mutations you see in the family tree. What we've done is work out a formula that corrects this effect so that we now have a reliable way of dating genetic lineages. "This means that we can put a timescale on any part of the particular family tree, right back to humanity's last common maternal ancestor, known as 'Mitochondrial Eve', who lived some 200,000 years ago. In fact we can date any migration for which we have available data," he says.

Moreover, working with a published database of more than 2,000 fully sequenced mtDNA samples, Soares' calculation, for the first time, uses data from the whole of the mtDNA molecule. This means that the results are not only more accurate, but also more precise, giving narrower date ranges.

The new method has already yielded some surprising findings. Says archaeogeneticist Professor Martin Richards, who supervised Soares: "We can settle the debate regarding mankind's expansion through the Americas. Researchers have been estimating dates from mtDNA that are too old for the archaeological evidence, but our calculations confirm the date to be some 15,000 years ago, around the time of the first unequivocal archaeological remains. "Furthermore, we can say with some confidence that the estimate of humanity's 'out of Africa' migration was around 60-70,000 years ago – some 10-20,000 years earlier than previously thought."

The team has devised a simple calculator into which researchers can feed their data and this is being made freely available on the University of Leeds website.

*The paper is published in the current edition of the American Journal of Human Genetics.*

### **Illness, medical bills linked to nearly two-thirds of bankruptcies: Harvard study**

#### **Harvard study finds 50 percent increase from 2001**

#### **Most of those bankrupted by illness were middle class and had insurance**

Medical problems contributed to nearly two-thirds (62.1 percent) of all bankruptcies in 2007, according to a study in the August issue of the American Journal of Medicine that will be published online Thursday. The data were collected prior to the current economic downturn and hence likely understate the current burden of financial suffering. Between 2001 and 2007, the proportion of all bankruptcies attributable to medical problems rose by 49.6 percent. The authors' previous 2001 findings have been widely cited by policy leaders, including President Obama.

Surprisingly, most of those bankrupted by medical problems had health insurance. More than three-quarters (77.9 percent) were insured at the start of the bankrupting illness, including 60.3 percent who had private coverage. Most of the medically bankrupt were solidly middle class before financial disaster hit. Two-thirds were homeowners and three-fifths had gone to college. In many cases, high medical bills coincided with a loss of income as illness forced breadwinners to lose time from work. Often illness led to job loss, and with it the loss of health insurance.

Even apparently well-insured families often faced high out-of-pocket medical costs for co-payments, deductibles and uncovered services. Medically bankrupt families with private insurance reported medical bills that averaged \$17,749 vs. \$26,971 for the uninsured. High costs - averaging \$22,568 - were incurred by those who initially had private coverage but lost it in the course of their illness.

Individuals with diabetes and those with neurological disorders such as multiple sclerosis had the highest costs, an average of \$26,971 and \$34,167 respectively. Hospital bills were the largest single expense for about half of all medically bankrupt families; prescription drugs were the largest expense for 18.6 percent.

The research, carried out jointly by researchers at Harvard Law School, Harvard Medical School and Ohio University, is the first nationwide study on medical causes of bankruptcy. The researchers surveyed a random sample of 2,314 bankruptcy filers during early 2007 and examined their bankruptcy court records. In addition, they conducted extensive telephone interviews with 1,032 of these bankruptcy filers.

Their 2001 study, which was published in 2005, surveyed debtors in only five states. In the current study, findings for those five states closely mirrored the national trends.

Subsequent to the 2001 study, Congress made it harder to file for bankruptcy, causing a sharp drop in filings. However, personal bankruptcy filings have soared as the economy has soured and are now back to the 2001 level of about 1.5 million annually.

Dr. David Himmelstein, the lead author of the study and an associate professor of medicine at Harvard, commented: "Our findings are frightening. Unless you're Warren Buffett, your family is just one serious illness away from bankruptcy. For middle-class Americans, health insurance offers little protection. Most of us have policies with so many loopholes, co-payments and deductibles that illness can put you in the poorhouse. And even the best job-based health insurance often vanishes when prolonged illness causes job loss - precisely when families need it most. Private health insurance is a defective product, akin to an umbrella that melts in the rain."

"For many families, bankruptcy is a deeply shameful experience," noted Elizabeth Warren, Leo Gottlieb Professor of Law at Harvard and a study co-author. Professor Warren, a leading expert on personal bankruptcy, went on: "People arrive at the bankruptcy courts exhausted - financially, physically and emotionally. For most, bankruptcy is a last choice to deal with unmanageable circumstances."

According to study co-author Dr. Steffie Woolhandler, an associate professor of medicine at Harvard and primary care physician in Cambridge, Mass.: "We need to rethink health reform. Covering the uninsured isn't enough. Reform also needs to help families who already have insurance by upgrading their coverage and assuring that they never lose it. Only single-payer national health insurance can make universal, comprehensive coverage affordable by saving the hundreds of billions we now waste on insurance overhead and bureaucracy. Unfortunately, Washington politicians seem ready to cave in to insurance firms and keep them and their counterfeit coverage at the core of our system. Reforms that expand phony insurance - stripped-down plans riddled with co-payments, deductibles and exclusions - won't stem the rising tide of medical bankruptcy."

Dr. Deborah Thorne, associate professor of sociology at Ohio University and study co-author, stated: "American families are confronting a panoply of social forces that make it terribly difficult to maintain financial stability - job losses and wages that have not kept pace with the cost of living, exploitation from the various lending industries, and, probably most consequential and disgraceful, a health care system that is so dysfunctional that even the most mundane illness or injury can result in bankruptcy. Families who file medical bankruptcies are overwhelmingly hard-working, middle-class families who have played by the rules of our economic system, and they deserve nothing less than affordable health care."

*A copy of the study is available at [http://www.pnhp.org/new\\_bankruptcy\\_study](http://www.pnhp.org/new_bankruptcy_study) or through the American Journal of Medicine, [ajmmedia@elsevier.com](mailto:ajmmedia@elsevier.com), (212) 633-3944. The authors have also prepared a supplementary "Fact Sheet" and a "Q&A" on medical bankruptcy, both of which detail the study's methods and findings. See same link above.*

*"Medical bankruptcy in the United States, 2007: Results of a national study," David U. Himmelstein, M.D.; Deborah Thorne, Ph.D.; Elizabeth Warren, J.D.; Steffie Woolhandler, M.D., M.P.H. American Journal of Medicine, June 4, 2009 (online).*

### **'Shock and kill' research gives new hope for HIV-1 eradication**

Latent HIV genes can be 'smoked out' of human cells. The so-called 'shock and kill' technique, described in a preclinical study in BioMed Central's open access journal *Retrovirology*, might represent a new milestone along the way to the discovery of a cure for HIV/AIDS.

Dr. Enrico Garaci, president of the Istituto Superiore di Sanità (the Italian Institute of Health) and Dr. Andrea Savarino, a retrovirologist working at the institution, worked with a team of researchers to study the so-called "barrier of latency" which has been the main obstacle to HIV eradication from the body.

Cells harbouring a quiescent HIV genome are responsible for HIV persistence during therapy. In other words, HIV-1 genes become pieces of the human organism, and many scientists have simply thought there is nothing we can do. Dr Savarino's team aimed to 'smoke out' the virus in order to render the latently infected

cells targetable by the immune system or artificial means. They write, "This can be achieved using inhibitors of histone deacetylases (HDACs), which are a class of enzymes that maintain HIV latency. However, their effects on HIV are evident only when used in toxic quantities".

To overcome this problem, the Italian researchers tested a collection of HDAC inhibitors, some of which specifically target only certain enzyme isoforms (class I HDACs) that are involved in HIV latency. The toxicity of this approach, however, was not markedly decreased, although it compromises a more limited number of cellular pathways. Moreover, at non-toxic quantities, class I HDAC inhibitors were able to induce the 'awakening' of a portion of cells within a latently infected cell population. The researchers then repeated the experiment adding a drug inducing oxidative stress, buthionine sulfoximine (BSO). The results showed that BSO recruited cells non-responsive to the HDAC inhibitors into the responding cell population. An important result was that the infected cells' 'awakening' was followed by cell death, whereas the non-infected cells were left intact by the drug combination.

"I really hope this study may open new avenues to the development of weapons able to eliminate the HIV-infected cells from the body", says Dr. Andrea Savarino, "Such weapons, in combination with antiretroviral therapies, could hopefully allow people living with HIV/AIDS to get rid of the virus and return to a normal life. Of note, there are testable drug combinations composed of molecules that have passed phase I clinical trials for safety in humans". This type of approach has been dubbed 'shock and kill'. "Although this type of approach is largely accepted by the scientific community", adds Dr. Savarino, "to be honest, we have to take into consideration that some scientists are skeptical about this approach, and others even think that a cure for HIV/AIDS will never be found. Experiments using animal models will shed a new light on this difficult problem."

### **One in four nursing home residents carries MRSA**

MRSA is a major problem in nursing homes with one in four residents carrying the bacteria, a study by Queen's University Belfast and Antrim Area Hospital has found.

Its authors say that the findings, which have been published in the Journal of the American Geriatrics Society, highlight the need for infection control strategies to be given a higher priority in nursing homes.

The study, funded by Health and Social Care Research and Development, Public Health Agency, Northern Ireland, thought to be the largest of its kind studying MRSA in private nursing homes in the UK, took nose swabs from 1,111 residents and 553 staff in 45 nursing homes in the former Northern Board area of Northern Ireland.

Twenty-four per cent of residents and 7 per cent of staff were found to be colonised with MRSA, meaning they were carrying the bacteria but not necessarily showing signs of infection or illness. Residents in 42 of the homes were colonised with MRSA, with recorded rates in individual nursing homes ranging from zero to 73 per cent.

Staff in 28 of the homes carried the bacteria with prevalence rates ranging from zero to 28 per cent. Dr Paddy Kearney, Consultant Medical Microbiologist with the Northern Health and Social Care Trust, said: "We decided to carry out the study after noticing an apparent increase in recent years in the number of patients who had MRSA when they were admitted to hospital from nursing homes. "In hospitals routine checks are carried out to identify those most at risk of MRSA colonisation (carrying it on their skin and/or nose) and infection control policies are put in place but this is not always feasible in private nursing homes."

Dr Michael Tunney, Senior Lecturer in Clinical Pharmacy, from Queen's University's School of Pharmacy, said: "This is the first study which has reported prevalence of MRSA among staff in nursing homes in the UK and found that staff need to be more aware of the potential problem MRSA can be in this setting."

Professor Carmel Hughes, a Director of Research in the School of Pharmacy, added: "In order to combat this problem, two approaches could be considered: improved education and training of staff, and removing MRSA from people who are colonised with it, using suitable creams and washes. "Further studies looking at these approaches need to be carried out."

### **Ancient warfare: Fighting for the greater good**

\* 19:00 04 June 2009 by Ewen Callaway

War, what is it good for? A lot, it could turn out. Lethal warfare drove the evolution of altruistic behaviour among ancient humans, claims a new study based on archaeological records and mathematical simulations.

If correct, the new model solves a long-standing puzzle in human evolution: how did our species transition from creatures interested in little more than passing down their own genes to societies of (generally) law-abiding (mostly) monogamists?

No one knows for sure when these changes happened, but climactic swings that occurred between approximately 10,000 to 150,000 years ago in the late Pleistocene period may have pushed once-isolated bands

of hunter-gatherers into more frequent contact with one another, says Samuel Bowles, an evolutionary biologist at the Santa Fe Institute in New Mexico and the University of Siena, Italy, who led the study. "I think that's just a recipe for high-level conflict."

### **Tribes at war**

By warfare, Bowles isn't talking about highly organised contests between nation-states and their armies. Rather, this period of warfare was probably characterised by ongoing skirmishes between neighbouring populations.

"We're talking about groups of men who got out in twos or threes or fives," he says. "They didn't have a chain of command and it's hard to see how they could force people to fight."

For this reason, altruistic intent on the part of each warrior is key. Each person would do better to stay home than to put their life on the line for their neighbours – yet they still went out and risked their lives, Bowles says.

To assess whether or not people with a random genetic predisposition to altruism could flourish via armed conflicts, Bowles culled archaeological and ethnographic data on the lethality of ancient warfare and plugged them into an evolutionary model of population change.



*Does a genetic predisposition to altruism flourish because of armed conflict?* (Image: Michael Friedel / Rex Features)

### **Cost of clashes**

In ancient graves excavated previously, Bowles found that up to 46 per cent of the skeletons from 15 different locations around the world showed signs of a violent death. More recently, war inflicted 30 per cent of deaths among the Ache, a hunter-gatherer population from Eastern Paraguay, 17 per cent among the Hiwi, who live in Venezuela and Colombia, while just 4 per cent among the Anbara in northern Australia. On average, warfare caused 14 per cent of the total deaths in ancient and more recent hunter-gatherers populations.

The cost of losing an armed conflict as a group is high enough to balance out the individual risks of warfare, especially if a population is relatively inbred, Bowles' model concludes. Since evolution acts on genes, it makes more sense to make more sacrifices for a related neighbour than an unrelated one.

Since Bowles had no way of knowing how inbred Pleistocene populations were, he compared contemporary hunter-gatherers such as African pygmies and native Siberians. Individuals in these populations were closely related enough to justify going to war, he found.

### **Inbreeding**

"There's no doubt that this is a controversial view," says Ruth Mace, an evolutionary anthropologist at University College London. Inbreeding between the victors and any surviving losers would dilute, not concentrate, altruistic genes, she says.

Bowles modelled this possibility in a previous paper and found that even with a measure of inbreeding, altruists still win out. However, he agrees that it would slow the evolution of altruism through warfare. "A much better way to spread the genes is to kill everybody," he says.

Mark van Vugt, a psychologist at the University of Kent at Canterbury, UK, notes that warriors could act in their own self-interest, not for the good of the group. "Studies on the Amazonian Yanomamö people show that these warriors do get a greater share of resources, they get more women, they sire more offspring," he says. "How do you explain that there are individual benefits for these warriors? There shouldn't be."

Still, van Vugt thinks Bowles' model is on the right track. Studies show that people divided into arbitrarily chosen groups – say heads and tails – behave altruistically to members of their group, but are more hostile toward non-members. "Together we provide different pieces of the puzzle. If they fit together, they are starting to make sense," van Vugt says. *Journal reference: Science (DOI: 10.1126/science.1168112)*

### **Donor organ 'personality' worry**

***Most people have a strong aversion to the idea of receiving a donor organ from a killer, a study suggests.***

Those questioned said they would be far happier receiving a transplant from someone with a good moral background, the Cheltenham Science Festival heard.

It follows on from research which found one in three organ transplant patients believe they have taken on some aspects of the donor's personality. Around 16m people are on the UK organ donor register.

Professor Bruce Hood, a cognitive neuroscientist at the University of Bristol, tested the effects of information about the morals of a potential donor in 20 students who were asked to imagine they needed a life-saving heart transplant. They were shown pictures of strangers and asked to rate how happy they would be to

receive an organ from them. The students were then shown the photos a second time but told that the person was good or bad. Negative scores increased dramatically when they were told the donor was a bad person.

When told they were looking at pictures of good people, there was a small increase in positive ratings.

The largest negative effect was for a murderer's heart.

### **'Connection'**

Professor Hood told the conference that he had spoken with patients who believe they have taken on a psychic connection with their organ donors, and even their memories and experiences.

"Some of the psychological changes many patients experience have very good physiological explanations, however according to one survey of transplant patients, approximately one in three attribute this change to taking on psychological characteristics of the donor even though conventional science has generally rejected the idea that such transference is possible."

He added that in one case, a British teenager was forcibly given a heart transplant against her will because she feared that she would be "different with someone else's heart". "This explains the findings that most people were repulsed by the thought of receiving a transplant from a murderer. "Essentially they believe they will somehow take on those characteristics of the donor."

Isabel Clarke, an NHS consultant clinical psychologist with an interest in spirituality said the association of ideas can be very powerful. "There's quite an emotional punch about the heart and receiving someone's heart."

A spokesman for NHS Blood and Transplant said organ donations were done anonymously in the UK so recipients would not know about the personality of the donor. "We ensure that organs donated for transplant are matched and allocated based on clinical need and criteria including, age, size, blood group and for kidneys, the tissue type. "Clinical analysis shows that these criteria are most relevant to the successful outcome of a transplant."

### **FSU study links 'warrior gene' to gang membership, weapon use**

TALLAHASSEE, Fla. -- Boys who carry a particular variation of the gene Monoamine oxidase A (MAOA), sometimes called the "warrior gene," are more likely not only to join gangs but also to be among the most violent members and to use weapons, according to a new study from The Florida State University that is the first to confirm an MAOA link specifically to gangs and guns.

Findings apply only to males. Girls with the same variant of the MAOA gene seem resistant to its potentially violent effects on gang membership and weapon use.

Led by noted biosocial criminologist Kevin M. Beaver at FSU's College of Criminology and Criminal Justice, the study sheds new light on the interplay of genetics and environment that produces some of society's most serious violent offenders.

"While gangs typically have been regarded as a sociological phenomenon, our investigation shows that variants of a specific MAOA gene, known as a 'low-activity 3-repeat allele,' play a significant role," said Beaver, an award-winning researcher who has co-authored more than 50 published papers on the biosocial underpinnings of criminal behavior.

"Previous research has linked low-activity MAOA variants to a wide range of antisocial, even violent, behavior, but our study confirms that these variants can predict gang membership," he said. "Moreover, we found that variants of this gene could distinguish gang members who were markedly more likely to behave violently and use weapons from members who were less likely to do either."

The MAOA gene affects levels of neurotransmitters such as dopamine and serotonin that are related to mood and behavior, and those variants that are related to violence are hereditary. Some previous studies have found the "warrior gene" to be more prevalent in cultures that are typified by warfare and aggression.

"What's interesting about the MAOA gene is its location on the X-chromosome," Beaver said. "As a result, males, who have one X-chromosome and one Y-chromosome, possess only one copy of this gene, while females, who have two X-chromosomes, carry two. Thus, if a male has an allele (variant) for the MAOA gene that is linked to violence, there isn't another copy to counteract it. Females, in contrast, have two copies, so even if they have one risk allele, they have another that could compensate for it. That's why most MAOA research has focused on males, and probably why the MAOA effect has, for the most part, only been detected in males."

The new study examined DNA data and lifestyle information drawn from more than 2,500 respondents to the National Longitudinal Study of Adolescent Health. Beaver and colleagues from Florida State, Iowa State and Saint Louis universities detailed their findings in a paper to be published in a forthcoming edition of the journal *Comprehensive Psychiatry*. Currently, the paper ("Monoamine oxidase A genotype is associated with gang membership and weapon use") is accessible online at [www.comppsyjournal.com](http://www.comppsyjournal.com) via the "Articles in Press" link.

In addition to the MAOA study, Beaver's body of biosocial criminology research includes published research that links genetics to adolescent victimization and formation of delinquent peer groups and the use of steroids to "roid rage" -- all among the first such works in the field. He won the American Society of Criminology's 2009 Ruth Shonle Cavan Young Scholar Award in recognition of his outstanding scholarly contributions during the short time since he earned a Ph.D. in criminal justice at the University of Cincinnati in 2006. Beaver is the coauthor/editor of "Biosocial Criminology: A Primer" (Kendall/Hunt, 2009) and six other books.