

[http://www.eurekalert.org/pub\\_releases/2011-04/sri-sdc041711.php](http://www.eurekalert.org/pub_releases/2011-04/sri-sdc041711.php)

## **Scientists develop compound that effectively halts progression of multiple sclerosis**

### ***The discovery also holds promise for other autoimmune disorders***

JUPITER, FL, – Scientists from the Florida campus of The Scripps Research Institute have developed the first of a new class of highly selective compounds that effectively suppresses the severity of multiple sclerosis in animal models. The new compound could provide new and potentially more effective therapeutic approaches to multiple sclerosis and other autoimmune diseases that affect patients worldwide. The study appeared April 17, 2011, in an advance online edition of the journal *Nature*.

Current treatments for autoimmunity suppress the patient's entire immune system, leaving patients vulnerable to a range of adverse side effects. Because the new compound, known as SR1001, only blocks the actions of a specific cell type playing a significant role in autoimmunity, it appears to avoid many of the widespread side effects of current therapies.

"This is a novel drug that works effectively in animal models with few side effects," said Tom Burriss, Ph.D., a professor in the Department of Molecular Therapeutics at Scripps Florida who led the study, which was a multidisciplinary collaboration with scientists including Patrick Griffin, William Roush, and Ted Kamenecka of Scripps Research, and Paul Drew of the University of Arkansas for Medical Sciences. "We have been involved in several discussions with both pharmaceutical and biotechnology firms who are very interested in developing it further." A lengthy process of drug development and review is required to ensure a new drug's safety and efficacy before it can be brought to market.

"This impressive multidisciplinary team has used a combined structural and functional approach to describe a class of molecules that could lead to new medicines for treating autoimmune diseases," said Charles Edmonds, Ph.D. who oversees structural biology grants at the National Institutes of Health. "Breakthroughs such as this highlight the value of scientists with diverse expertise joining forces to solve important biological problems that have the potential to benefit human health."

### **Targeting Specific Receptors**

For the past several years, Burriss and his colleagues have been investigating small-molecule compounds that affect particular disease-related receptors (structures that bind other molecules, triggering some effect on the cell). In particular, the scientists have been interested in a pair of "orphan nuclear receptors" (receptors with no known natural binding partner) called ROR $\alpha$  and ROR $\gamma$  involved in both autoimmune and metabolic diseases.

These particular receptors play a critical role in the development of TH17 cells, a form of T helper cells that make up part of the immune system. A relatively new discovery, TH17 cells have been implicated in the pathology of numerous autoimmune diseases, including multiple sclerosis, rheumatoid arthritis, inflammatory bowel disease, and lupus. TH17 cells produce Interleukin-17, a natural molecule that can induce inflammation, a characteristic of autoimmunity.

"If you eliminate TH17 cell signals, you basically eliminate the disease in animal models," Burriss said. "Our compound is the first small-molecule orally active drug that targets this specific cell type and shuts it down. Once SR1001 is optimized, chances are it will be far more potent and effective." The compound works without affecting other types of T helper cells and without any significant metabolic impact, Burriss added.

*The first author of the study, "Inhibition of TH17 Differentiation and Suppression of Autoimmunity by a Selective Synthetic ROR Ligand," is Laura A. Solt of Scripps Research. In addition to Burriss, Griffin, Roush, Kamenecka, Drew, and Solt, other authors include Naresh Kumar, Philippe Nuhant, Yongjun Wang, Janelle L. Lauer, Jin Liu, and Monica Istrate of Scripps Research; Dušica Vidović, Stephan C. Schürer of Scripps Research and the Center for Computational Science, University of Miami; and Jihong Xu and Gail Wagoner of the University of Arkansas for Medical Sciences. See <http://www.nature.com/nature/journal/vaop/ncurrent/abs/nature10075.html>.*

*The study was supported by the National Institutes of Health's National Institute of General Medical Sciences, National Institute of Diabetes and Digestive and Kidney Diseases, and National Institute of Mental Health.*

[http://www.eurekalert.org/pub\\_releases/2011-04/s-tpo041811.php](http://www.eurekalert.org/pub_releases/2011-04/s-tpo041811.php)

## **The pain of evolution: A big toothache for reptiles**

### ***Study reveals infection in the jaw of 275-million-year-old reptile, highlighting the high cost of having permanent teeth***

Our susceptibility to oral infection has some parallels to those of ancient reptiles that evolved to eat a diet incorporating plants in addition to meat. That's according to Robert Reisz from the University of Toronto and his colleagues who found evidence of bone damage due to oral infection in Paleozoic reptiles as they adapted to living on land. Their findings, published online in Springer's journal *Naturwissenschaften - The Nature of Science*, predate the previous record for oral and dental disease in a terrestrial vertebrate by nearly 200 million years.

The researchers investigated the jaws of several well-preserved specimens of *Labidosaurus hama-tus*, a 275-million-year-old terrestrial reptile from North America. One specimen stood out because of missing teeth and associated erosion of the jaw bone. With the aid of CT-scanning, Reisz and colleagues found evidence of a massive infection. This resulted in the loss of several teeth, as well as bone destruction in the jaw in the form of an abscess and internal loss of bone tissue.

As the ancestors of advanced reptiles diversified to life on land, many evolved dental and cranial specializations to feed more efficiently on other animals and to incorporate high-fiber plant leaves and stems into their diet. The primitive dental pattern in which teeth were loosely attached to the jaws and continuously replaced, changed in some lineages to be strongly attached to the jaw, with little or no tooth replacement. This was clearly advantageous to some early reptiles, allowing them to chew their food and thus improve nutrient absorption. The abundance and global distribution of *Labidosauris* and its kin attest to the evolutionary success of this strategy.

However, Reisz and his colleagues suggest that as this reptile lost the ability to replace teeth, the likelihood of infections of the jaw, resulting from damage to the teeth, increased substantially. This is because prolonged exposure of the dental pulp cavity of heavily worn or damaged teeth to oral bacteria was much greater than in other animals that quickly replaced their teeth. The authors conclude: "Our findings allow us to speculate that our own human system of having just two sets of teeth, baby and permanent, although of obvious advantage because of its ability to chew and process many different foodstuffs, is more susceptible to infection than that of our distant ancestors that had a continuous cycle of tooth replacement."

#### Reference

1. Reisz R R et al (2011). *Osteomyelitis in a Paleozoic reptile: ancient evidence for bacterial infection and its evolutionary significance*. *Naturwissenschaften – The Nature of Science*. DOI 10.1007/s00114-011-0792-1

[http://www.eurekalert.org/pub\\_releases/2011-04/uop-prc041811.php](http://www.eurekalert.org/pub_releases/2011-04/uop-prc041811.php)

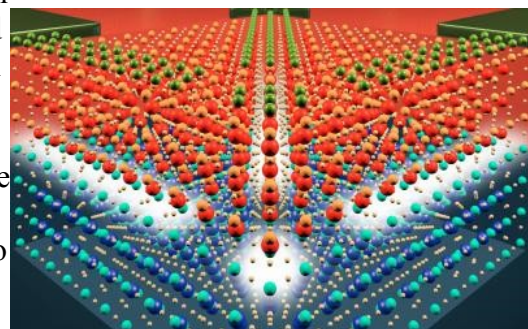
### **Pitt-led researchers create super-small transistor, artificial atom powered by single electrons**

#### ***A team from Pitt, UW-Madison and HP Labs reports in Nature Nanotechnology a 1.5-nanometer single-electron transistor that could lead to long-lasting, ultradense computer memories, quantum computers and advanced electronics***

PITTSBURGH - A University of Pittsburgh-led team has created a single-electron transistor that provides a building block for new, more powerful computer memories, advanced electronic materials, and the basic components of quantum computers.

The researchers report in *Nature Nanotechnology* that the transistor's central component - an island only 1.5 nanometers in diameter - operates with the addition of only one or two electrons. That capability would make the transistor important to a range of computational applications, from ultradense memories to quantum processors, powerful devices that promise to solve problems so complex that all of the world's computers working together for billions of years could not crack them.

In addition, the tiny central island could be used as an artificial atom for developing new classes of artificial electronic materials, such as exotic superconductors with properties not found in natural materials, explained lead researcher Jeremy Levy, a professor of physics and astronomy in Pitt's School of Arts and Sciences. Levy worked with lead author and Pitt physics and astronomy graduate student Guanglei Cheng, as well as with Pitt physics and astronomy researchers Feng Bi, Daniela Bogorin, and Cheng Cen. The Pitt researchers worked with a team from the University of Wisconsin at Madison led by materials science and engineering professor Chang-Beom Eom, including research associates Chung Wun Bark, Jae-Wan Park, and Chad Folkman. Also part of the team were Gilberto Medeiros-Ribeiro, of HP Labs, and Pablo F. Siles, a doctoral student at the State University of Campinas in Brazil.



***An atomic-scale depiction of the SketchSET shows three wires (green bars) converging on the central island (center green area), which can house up to two electrons. Electrons tunnel from one wire to another through the island. Conditions on the third wire can result in distinct conductive properties. U. Pittsburgh***

Levy and his colleagues named their device SketchSET, or sketch-based single-electron transistor, after a technique developed in Levy's lab in 2008 that works like a microscopic Etch A Sketch™, the drawing toy that inspired the idea. Using the sharp conducting probe of an atomic force microscope, Levy can create such electronic devices as wires and transistors of nanometer dimensions at the interface of a crystal of strontium

titanate and a 1.2 nanometer thick layer of lanthanum aluminate. The electronic devices can then be erased and the interface used anew.

The SketchSET - which is the first single-electron transistor made entirely of oxide-based materials - consists of an island formation that can house up to two electrons. The number of electrons on the island - which can be only zero, one, or two - results in distinct conductive properties. Wires extending from the transistor carry additional electrons across the island.

One virtue of a single-electron transistor is its extreme sensitivity to an electric charge, Levy explained. Another property of these oxide materials is ferroelectricity, which allows the transistor to act as a solid-state memory. The ferroelectric state can, in the absence of external power, control the number of electrons on the island, which in turn can be used to represent the 1 or 0 state of a memory element. A computer memory based on this property would be able to retain information even when the processor itself is powered down, Levy said. The ferroelectric state also is expected to be sensitive to small pressure changes at nanometer scales, making this device potentially useful as a nanoscale charge and force sensor.

Since August 2010, Levy has led a \$7.5 million, multi-institutional project to construct a semiconductor with properties similar to SketchSET, he said. Funded by the U.S. Air Force Office of Scientific Research's Multi-University Research Initiative (MURI) program, the five-year effort is intended to overcome some of the most significant challenges related to the development of quantum information technology. Levy works on that project with researchers from Cornell, Stanford, the University of California at Santa Barbara, the University of Michigan, and UW-Madison.

*The research in Nature Nanotechnology also was supported in part by grants from the U.S. Defense Advanced Research Projects Agency (DARPA), the U.S. Army Research Office, the National Science Foundation, and the Fine Foundation.*

[http://www.eurekalert.org/pub\\_releases/2011-04/aaon-scv041211.php](http://www.eurekalert.org/pub_releases/2011-04/aaon-scv041211.php)

### **Study: Common virus + low sunlight exposure may increase risk of MS**

**ST. PAUL, Minn. – New research suggests that people who are exposed to low levels of sunlight coupled with a history of having a common virus known as mononucleosis may be at greater odds of developing multiple sclerosis (MS) than those without the virus.**

The research is published in the April 19, 2011, print issue of *Neurology*®, the medical journal of the American Academy of Neurology. "MS is more common at higher latitudes, farther away from the equator," said George C. Ebers, MD, with the University of Oxford in the United Kingdom and a member of the American Academy of Neurology. "Since the disease has been linked to environmental factors such as low levels of sun exposure and a history of infectious mononucleosis, we wanted to see whether the two together would help explain the variance in the disease across the United Kingdom."

Infectious mononucleosis is a disease caused by the Epstein-Barr virus, which is a Herpes virus that is extremely common but causes no symptoms in most people. However, when a person contracts the virus as a teenager or adult, it often leads to infectious mononucleosis. The body makes vitamin D when exposed to ultraviolet B (UVB) light.

For the study, researchers looked at all hospital admissions to National Health Service hospitals in England over seven years. Specifically, they identified 56,681 cases of multiple sclerosis and 14,621 cases of infectious mononucleosis. Scientists also looked at NASA data on ultraviolet intensity in England.

The study found that adding the effects of sunlight exposure and mononucleosis together explained 72 percent of the variance in the occurrence of MS across the United Kingdom. Sunlight exposure alone accounted for 61 percent of the variance. "It's possible that vitamin D deficiency may lead to an abnormal response to the Epstein-Barr virus," Ebers said.

He noted that low sunlight exposure in the spring was most strongly associated with MS risk. "Lower levels of UVB in the spring season correspond with peak risk of MS by birth month. More research should be done on whether increasing UVB exposure or using vitamin D supplements and possible treatments or vaccines for the Epstein-Barr virus could lead to fewer cases of MS."

*The study was supported by the Multiple Sclerosis Society of Great Britain and Northern Ireland, the Medical Research Council and the Wellcome Trust.*

[http://www.eurekalert.org/pub\\_releases/2011-04/uom-mso041811.php](http://www.eurekalert.org/pub_releases/2011-04/uom-mso041811.php)

### **Mood swings of bipolar patients can be predicted, study shows**

**The future mood swings of people with bipolar disorder can be predicted by their current thoughts and behaviour, a study published today (Tuesday) has found.**

Psychologists from the Universities of Manchester and Lancaster say their findings are important because they mean talking therapies, like cognitive behavioural therapy (CBT), could prove effective treatments for the condition.

People with bipolar are prone to extreme mood swings that take them from great emotional highs to the pits of depression; the cause of these mood swings is often put down to the patients' genes and biology rather than their own thoughts and actions.

For this latest study – published in the American Psychological Association journal *Psychological Assessment* – the researchers followed 50 people with bipolar disorder for a month. The team found that the patients' thinking and behaviour predicted their future mood swings even when their medical history had been accounted for.

"Individuals who believed extreme things about their moods – for example that their moods were completely out of their own control or that they had to keep active all the time to prevent becoming a failure – developed more mood problems in a month's time," said study lead Dr Warren Mansell, in Manchester's School of Psychological Sciences. "In contrast, people with bipolar disorder who could let their moods pass as a normal reaction to stress or knew they could manage their mood, fared well a month later. These findings are encouraging for talking therapies – such as CBT – that aim to help patients to talk about their moods and change their thinking about them."

A new form of CBT, known as TEAMS (Think Effectively About Mood Swings), is being developed by Dr Mansell and colleagues, at The University of Manchester. It aims to improve on previous therapies by focusing on current problems, like depression, anxiety and irritability, and helping patients to set goals for their life as a whole.

The aim of this new approach is to encourage patients to accept and manage a range of normal emotions – like joy, anger and fear – and a controlled trial is about to start following a successful case series of the TEAMS approach. The researchers will use the TEAMS approach to follow up their current findings with a larger study that identifies who relapses and who heads towards recovery in the long term.

*Notes for editors:*

*A copy of the paper, entitled 'Extreme Appraisals of Internal States and Bipolar Symptoms: The Hypomanic Attitudes and Positive Predictions Inventory,' published in the ASA's Psychological Assessment journal, is available on request.*

[http://www.eurekalert.org/pub\\_releases/2011-04/osu-fts041811.php](http://www.eurekalert.org/pub_releases/2011-04/osu-fts041811.php)

### **For testing skin cream, synthetic skin may be as good as the real thing**

**COLUMBUS, Ohio – New research suggests that currently available types of synthetic skin may now be good enough to imitate animal skin in laboratory tests, and may be on their way to truly simulating human skin in the future.**

Researchers compared the response of synthetic skins to rat skin when they were both exposed to a generic skin cream treatment, and the results indicated they both reacted similarly.

The scientists used high-resolution images of two types of synthetic skin and samples of rat skin to discover similarities on microscopic scales. The findings have implications for the treatment of burn victims.

When a person's body is severely burned, he or she may not have enough healthy skin remaining to attempt healing the burns through skin cell regeneration with his or her own skin. In this case, synthetic skin or animal skin provides a potential substitute. But the use of animal skin comes with a variety of problems.

"In addition to ethical issues, animal skin is hard to obtain, expensive, and gives highly variable results because of individual skin variability," said Bharat Bhushan, Ohio Eminent Scholar and the Howard D. Winbigger Professor of mechanical engineering at Ohio State University. "Animal skin will vary from animal to animal, which makes it hard to anticipate how it might affect burnt victims, individually," Bhushan said. "But, synthetic skin's composition is consistent, making it a more reliable product," he continued.

Bhushan's research will appear in the June 5 issue of the *Journal of Applied Polymer Science*.

Bhushan and his colleague Wei Tang, an engineer at China University of Mining and Technology, compared two different types of synthetic skin to rat skin. The first synthetic skin was a commercially available skin purchased from Smooth-On, Inc. of Easton, Pennsylvania. The second synthetic skin was produced in Bhushan's lab. Ohio State's University Lab Animal Resources provided the rat skin samples.

Whether a synthetic skin feels and acts like real skin is very important, Bhushan explained. The skin must stand up to environmental effects such as sunlight or rain, while maintaining its texture and consistency. Scientists have continued to improve the practical and aesthetic properties of synthetic skin, which suggests it may soon be ready to replace animal skin and, farther in the future, human skin.

"Right now, our main concern is to determine whether the synthetic skin behaves like any real skin. Then, scientists can go on to more complex problems like modeling synthetic products that behave exactly like human skin," Bhushan said.

Bhushan is an expert at measuring effects on tiny scales, such as a nanometer, or billionth of a meter, which is important in skin research.

"Cellular events, like the effective and accurate delivery of drugs and the absorption of skincare products – these things occur at the nanoscale," explained Bhushan.

Using a highly sensitive microscope, known as an atomic force microscope, Bhushan and Tang were able to view the skin and the affects of an applied skin cream on a scale of about 100 nanometers. The average width of a human hair is approximately 1,000 times larger.

Despite the difference in surface features between the two synthetic skins and rat skin, the skin-cream had a comparable affect on all three samples. "The skin cream reduced the surface roughness, increased the skin's ability to absorb moisture from the environment, and softened the skin surface," said Bhushan.

Even before the addition of the skin cream, the synthetic and rat skins appeared comparable. Although the synthetic skins lacked hair follicles, they had similar roughness, meaning the distance between the highest point and lowest points on the skins' surfaces were similar.

"After treatment with skin cream, the trends of the peak-to-valley distance of the two synthetic skins and rat skin were the same, and both of them decreased. This indicates the skin cream treatment smoothed the skin surface," said Bhushan.

Bhushan explains that their future work will involve improving testing methods for measuring certain properties such as surface roughness. They also want to test a different skin cream.

[http://www.eurekalert.org/pub\\_releases/2011-04/jaaj-doa041511.php](http://www.eurekalert.org/pub_releases/2011-04/jaaj-doa041511.php)

### **Do-not-resuscitate orders associated with poor surgical outcomes even for non-emergency procedures**

***Surgical patients with do-not-resuscitate (DNR) orders appear to be at higher risk for poor surgical outcomes, according to a report published online today by the Archives of Surgery, one of the JAMA/Archives journals. The study will appear in the August print issue of the journal.***

"Do-not-resuscitate (DNR) orders preclude the use of cardiopulmonary resuscitation (CPR) in a clinically unresponsive, pulseless patient," according to background information provided by the authors. Approximately 70 percent of patients in the United States die with a DNR order. "Patients with a DNR order consent to a variety of surgical procedures ranging from palliative surgery to aggressive attempts at extension of life. The goals of surgical interventions in such patients include gaining 'additional time,' improving quality of life, decreasing pain, or treating isolated problems, such as fracture." The authors note that the use of DNR orders has been increasing and now up to 15 percent of patients with a DNR order have surgery.

Hadiza Kazaure, B.Sc., and colleagues from Yale University School of Medicine, New Haven, Conn., analyzed data from the more than 120 hospitals participating in the American College of Surgeons Quality Improvement Program from 2005 to 2008. There were 4,128 adult patients with DNR orders and 4,128 age-matched and procedure-matched patients without DNR orders. The main outcome measured were occurrence of one or more post-operative complication, re-operation, death within 30 days of surgery, total time in the operating room and length of stay. The majority of patients were elderly white women (average age, 79 years).

"The overall mortality rate was 15.3 percent," the authors report. "Compared with non-DNR patients, more than twice as many DNR patients died within 30 days of surgery (8.4 percent vs 23.1 percent). The DNR patients were more likely to die regardless of the urgency of the surgical procedure (35.5 percent vs. 17.8 percent and 16.6 percent vs. 5.5 percent for emergent and non-emergent procedures, respectively)." The authors found that patients with DNR orders were more likely to die after every procedure analyzed; after adjustment for multiple risk factors, a DNR order was associated with an increased odds of death. The authors note the overall complication rate was 28.6 percent. "The DNR patients had higher complication rates than non-DNR patients (31 percent vs. 26.4 percent)."

"The DNR patients may have surgery to gain 'additional time'; nevertheless, our study demonstrates that almost a quarter of DNR patients die within 30 days of surgery. Informed consent and elicitation of the goals of surgery, especially as they relate to overall goals of care, are essential for guiding surgical decisions involving DNR patients and their families. Issues pertaining to DNR status are complex, and they should be anticipated long before the 30-day period leading to an operation. Additional research is needed to evaluate the decision making of DNR patients with respect to undergoing surgery, particularly in the non-emergent setting, and the impact of a pre-operative DNR order on post-operative surgical care and to determine the long-term outcomes of DNR patients by procedure," the authors conclude.

*(Arch Surg. Published Online April 18, 2011. doi:10.1001/archsurg.2011.60. Available pre-embargo to the media at [www.jamamedia.org](http://www.jamamedia.org).)*

*Editor's Note: This study was supported in part by the Yale Medical Student Research Fellowship (Ms. Kazaure). Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.*

### **Cell of origin for squamous cell carcinoma discovered**

***Squamous cell cancers, which can occur in multiple organs in the body, can originate from hair follicle stem cells, a finding that could result in new strategies to treat and potentially prevent the disease, according to a study by researchers with UCLA's Jonsson Comprehensive Cancer Center and the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA.***

Researchers also found that the progeny of those cells, although just a few divisions away from the mother hair follicle stem cells, were not capable of forming squamous cell cancers. Further studying why those progeny, called transit amplifying cells, can't develop cancer could provide vital clues to how squamous cell cancers originate, said William Lowry, an assistant professor of molecular, cell and developmental biology in Life Sciences and senior author of the study.

The study, conducted in mouse models, appears the week of April 18 in the early online edition in the peer-reviewed journal the Proceedings of the National Academy of Sciences (PNAS).

It had been suggested in the literature that squamous cell cancers could arise from the hair follicle, but it was not clear what cell type within the follicle was responsible. This is the first time two distinct cell types in the skin have been compared and contrasted for their ability to develop squamous cell cancers, said Lowry, who is a Jonsson Cancer Center and Broad Stem Cell Research Center scientist.

"It was surprising that the progeny of these stem cells, which are developmentally more restricted, could not develop cancers when the mother stem cells could," said Lowry. "There is something fundamentally different between the two, and it's important that we figure out why one type of cell was able to develop cancer and the other was not. The insights we gain will tell us how these cancers arise in the first place, and could provide us with a wealth of novel targets we could go after to prevent the cancer before it starts."

A type of non-melanoma skin cancer, these cancers form in squamous cells, thin, flat cells found on the surface of the skin, the lining of the hollow organs of the body and the passages of the respiratory and digestive tracts. Squamous cell cancers occur in the skin, lips, mouth, esophagus, bladder, prostate, lungs, vagina, anus and cervix. Despite the common name, these cancers are unique malignancies with significant differences in manifestation and prognosis.

In this study, Lowry and his team sought to determine which cells of the epidermis, or skin, could give rise to squamous cell cancer. They wanted to find out if skin stem cells had properties that made them more prone to develop tumors than non-stem cells, said Andrew White, a post-doctoral fellow in Lowry's lab and first author of the study.

"Adult stem cells are long-lived and can acquire mutations that can cause cancer, but they also have intrinsic properties for self-renewal that are similar to cancer that could make them more tumor prone," White said.

Lowry and his team delivered genetic hits – adding an oncogene that is known to cause cancer and removing a tumor suppressor gene - to the hair follicle stem cells and the transit amplifying cells in two groups of mice and waited to see which developed cancer. Only the mice that received the genetic hits in the hair follicle stem cell population developed squamous cell cancer.

Going forward, White will molecularly profile the hair follicle stem cells and the transit amplifying cells to determine what string of biologic events occur when the cancer-causing genes are delivered. The differences between the two will be illuminating, Lowry said. "We hope that this will lead to much more specific therapies that target cancer initiation rather than treating the disease once it's established," Lowry said. "If we're lucky, a drug may already exist that will hit a target we identify."

The four-year study was funded by the Jonsson Cancer Center Foundation, a training grant from the California Institute for Regenerative Medicine, the National Institutes of Health, the American Cancer Society, the University of California Cancer Research Coordinating Committee and the Maria Rowena Ross Chair in Cell Biology and Biochemistry. A Belgium-based team also came to similar conclusions using slightly different methods, confirming the UCLA results. That study is published alongside Lowry's in PNAS.

### **Marine organisms with eternal life can solve the riddle of aging**

***Animals that reproduce asexually by somatic cloning have special mechanisms that delay ageing provide exceptionally good health.***

Scientists at the University of Gothenburg have shown how colony-forming ascidians (or sea squirts) can activate the enzyme telomerase, which protects DNA. This enzyme is more active also in humans who attain an advanced age. "Animals that clone themselves, in which part of an individual's body is passed on to the next generations, have particularly interesting conditions related to remaining in good health to persist. This makes it

useful to study these animals in order to understand mechanisms of ageing in humans", says Helen Nilsson Sköld of the Department of Marine Ecology, University of Gothenburg.

There are enormous differences in the lengths of life of the Earth's species. Some animals and plants that reproduce asexually can in principle achieve essentially eternal life; there are examples of deep-sea corals that are tens of thousands of years old. Helen Nilsson Sköld has decided to study sea squirts and starfish, which are species whose genes resemble closely those of humans.

"My research has shown that sea squirts rejuvenate themselves by activating the enzyme telomerase, and in this way extending their chromosomes and protecting their DNA. They also have a special ability to discard 'junk' from their cells. Older parts of the animal are quite simply broken down, and are then partially recycled when new and healthy parts grow out from the adult bodies."

Some species of starfish reproduce asexually by tearing apart their bodies, while others reproduce sexually only. This makes them particularly interesting animals to study. Both types of starfish can reconstruct lost body parts, but the species that reproduce asexually have considerably better health.

However, one consequence of asexual reproduction is that the species as a whole will have a very low genetic variation. This means that they will be particularly vulnerable to climate change, and the subsequent new types of changes in the environment. There is a high risk that these animals and plants will lose out – and then we will lose important knowledge about the riddle of ageing.

<http://www.scientificamerican.com/blog/post.cfm?id=early-human-fossils-from-south-afri-2011-04-18>

### Early human fossils from South Africa could upend longheld view of human evolution

By Kate Wong | Monday, April 18, 2011 | 25

**MINNEAPOLIS - It's a great irony of paleoanthropology that for all the insights scientists have been able to glean from the fossil record about our early ancestors, the australopithecines (Lucy and her kin), they have precious little to document the origin of our own genus, Homo.**

They know that Homo descended from one of those australopithecine species and that over the course of that transition our ancestors evolved from chimp-size creatures with short legs and small brains into tall humans with long legs and large brains, among other hallmark traits. But the details of this evolutionary transformation - when the distinctive Homo characteristics arose and why - have remained elusive, because fossils of early Homo are rare and the ones that have turned up are generally too fragmentary to yield much information.

To that end, last spring Lee Berger of the University of the Witwatersrand in Johannesburg, South Africa, and his colleagues announced their discovery of two partial human skeletons (pictured above) from that mysterious period that might well revolutionize researcher's understanding of how our genus got its start. The specimens, which date to around 1.95 million years ago, were said to exhibit a mosaic of traits linking them to both Australopithecus and Homo, leading the team to propose that they represent a previously unknown species of human - Australopithecus sediba - that could be the direct ancestor of Homo. The interpretation was controversial. Some critics argued that the fossils do belong in Australopithecus, but have no special relationship to Homo; others contended that they represent a dead-end branch of Homo, rather than ancestor of later species, including H. sapiens.

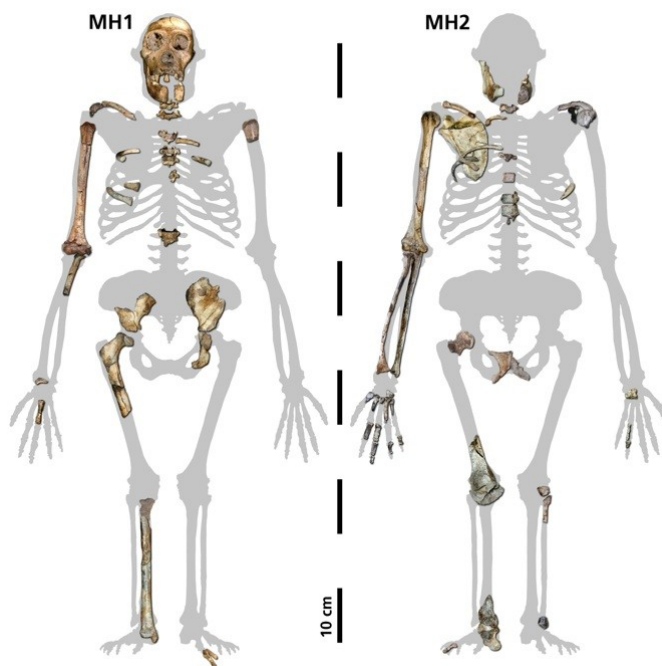


Image: skeletons courtesy of Science/AAAS

On April 12 at the annual meeting of the Paleoanthropology Society and on April 16 at the annual meeting of the American Association of Physical Anthropologists, Berger and his colleagues gave presentations on the results of their latest analyses of the A. sediba bones. The findings underscore the mosaic nature of the remains, and threaten to topple a leading model of human evolution.

Team member Kristian J. Carlson talked about the shape of A. sediba's brain, as revealed by synchrotron scanning of the interior of the brain case. With an estimated cranial capacity of just 420 cubic centimeters, this species had about a third as much gray matter as we do. Indeed this tiny brain size - which lies in the lower end of the Australopithecus range - figured significantly in the team's decision to place the fossils in the genus

Australopithecus rather than Homo. Yet despite the diminutive size of the brain, its frontal lobe appears to have had a much more humanlike organization than that of the australopithecines. Carlson noted that this surprising finding hints that frontal lobe reorganization and the overall increase in brain size that characterizes Homo may not have occurred simultaneously, as was thought.

The mixture of primitive and advanced traits is apparent throughout the skeleton. Darryl de Ruiter of Texas A&M University reported that the skull exhibits a suite of traits in common with australopithecines, particularly *A. africanus*. Yet it also shares a number of skull traits in common with Homo - more, in fact, than any other australopithecine does. "The combination of primitive and derived cranial and postcranial [below the neck] characteristics in *sediba* highlight its intermediate nature," de Ruiter observed, reiterating the team's earlier claim that *A. sediba* could be the ancestor of Homo. Berger enumerated other mosaic traits - including the apelike ribcage and long arms combined with the humanlike hand, with its short fingers and long thumb.

But it was the pelvis of *A. sediba* that yielded perhaps the most startling revelation at the meetings. Many researchers have argued that increasing brain size in the Homo lineage was the driving factor in the evolution of the Homo pelvis from the australopithecine one, because in early Homo fossils a larger braincase accompanies the modified pelvis. According to a talk given by Berger on behalf of Steven Churchill of Duke University, however, *A. sediba*, with its tiny brain, has a pelvis that looks a lot like that of early Homo.

If ballooning brain size was not the driving factor in evolving a humanlike pelvis, then what was? "I would say it's the shift from habitual bipedalism to more humanlike obligate bipedal locomotion," Will Harcourt-Smith of the American Museum of Natural History in New York City, an expert not involved in the analysis, told *Scientific American*. He thinks bipedalism probably evolved in two stages: in the first stage, represented by Lucy's species, early humans still spent a fair amount of time climbing in the trees in addition to walking upright on the ground. In the second, they lost their climbing ability and became fully bipedal.

"It's very reasonable to see [*A. sediba*] as the ancestor of Homo," Harcourt-Smith remarked, noting that he was much more on the fence until he saw the pelvis. "Am I 100 percent convinced? No, but it's persuasive."

[http://www.eurekalert.org/pub\\_releases/2011-04/uoc - acm041511.php](http://www.eurekalert.org/pub_releases/2011-04/uoc - acm041511.php)

### **A cancer marker and treatment in 1?**

#### ***UC San Diego researchers finds promise in non-human sialic acid antibodies***

Researchers at the University of California, San Diego School of Medicine say antibodies to a non-human sugar molecule commonly found in people may be useful as a future biomarker for predicting cancer risk, for diagnosing cancer cases early and, in sufficient concentration, used as a treatment for suppressing tumor growth.

The work was led by Richard Schwab, MD, assistant clinical professor of medicine, and Ajit Varki, MD, professor of medicine and cellular and molecular medicine, with other faculty at the UCSD Moores Cancer Center and the UCSD Glycobiology Research and Training Center. Collaborators include researchers from the groups of Xi Chen at UC Davis, Inder Verma at the Salk Institute and scientists from Sialix, Inc., a biotechnology company based in Vista, CA.

It is published in the April 19 online issue of the journal *Cancer Research* and in the May 1 print edition.

Every animal cell is cloaked in complex molecules called sialic acids that serve as vital contact points for interaction with other cells and the surrounding environment. Humans produce a particular kind of sialic acid called N-acetylneuraminic acid (Neu5Ac), but can also carry another non-human type called N-glycolylneuraminic acid or Neu5Gc, which is obtained through the diet, notably by the consumption of red meat. The molecular structures of these sialic acids differ by just a single oxygen atom, but this difference is enough to prompt the human immune system to produce a complex anti-Neu5Gc response.

In previous research, Varki and colleagues described how low-dose anti-Neu5Gc antibodies can lead to chronic inflammation, an immunological response associated with cancer development and growth.

In the new work, using a novel sialoglycan-microarray, the team discovered that patients with carcinomas have elevated levels of antibodies to one specific Neu5Gc-containing sugar chain. This unusual antigen arises from dietary Neu5Gc incorporation into the cancer marker Sialyl-Tn. It is the first example of a biomarker in the form of human "xeno-autoantibodies" to a dietary molecule.

Following up on this discovery, the scientists also found that purified human anti-Neu5Gc antibodies have immunotherapeutic potential: they specifically kill Neu5Gc-expressing mouse or human tumors when applied at higher concentrations. These findings point to a dual response of anti-Neu5Gc antibodies that can either stimulate tumor growth at a low dose (serving as a biomarker of disease) or suppress tumor growth at a high dose.

"Precisely how therapeutic antibodies work in patients remains unclear, even in therapies already approved by the Food and Drug Administration," said Schwab. "It is likely a combination of signaling immune cells to



kill cancer cells and antibodies directly killing cells by recruiting other proteins in the body. Understanding how lower levels of antibodies stimulate cancer growth while strong responses can kill cancer cells will be critical to moving this approach safely into cancer treatment."

Schwab noted that many questions and much research remains to be done. Long-term studies are required to learn whether levels of anti-Neu5Gc antibodies are a reliable indicator of future cancer risk, if this risk can be reduced, and if they can be used for early detection of cancers. Developing these antibodies as cancer treatments will require further study of how exactly the antibodies act against Neu5Gc-expressing tumors.

Nonetheless, Schwab expressed optimism about the significance and future of the work.

"This is the first evidence that anti-Neu5Gc antibodies may be useful for the early detection of cancer, identifying cancer risk, or for treatment," he said. "The biggest problem with advancing this work is that sugars are inherently difficult to study, but more people are beginning to pay attention – including the National Cancer Institute, which organized a specific multi-institute glycomics program that funded our project. A blood test that could detect cancer early or identify a modifiable risk for cancer would be a tremendous breakthrough in cancer care."

*Co-authors of the paper are Vered Padler-Karavani, Patrick Secrest, Yu-Tsueng Liu and Karen Messer of the UCSD Glycobiology Research and Training Center and UCSD Moores Cancer Center; Nancy Hurtado-Ziola and Darius Ghaderi, Sialix, Inc., Vista, CA; Hai Yu, Shengshu Huang, Saddam Muthana, Harshal A. Chokhawala, Hongzhi Cao and Xi Chen, Department of Chemistry, University of California, Davis; Dinorah Friedmann-Morvinski, Oded Singer and Inder M. Verma, Laboratory of Genetics, Salk Institute for Biological Studies.*

*Declaration: Varki is co-founder of Sialix, Inc., a startup biotech company focused on solving problems arising from Neu5Gc contamination of foods and drugs, and which has licensed the technology from UC San Diego. Nancy Hurtado-Ziola and Darius Ghaderi are presently full-time employees of Sialix. None of the other authors have a personal financial interest in any companies whose products are studied or mentioned.*

[http://www.eurekalert.org/pub\\_releases/2011-04/cp-cmr041811.php](http://www.eurekalert.org/pub_releases/2011-04/cp-cmr041811.php)

## **Cardiac muscle really knows how to relax: Potential cardio-protective mechanism in heart**

### ***New insight into the physiology of cardiac muscle may lead to the development of therapeutic strategies that exploit an inherent protective state of the heart.***

The research, published by Cell Press online on April 19th in the Biophysical Journal, discovers a state of cardiac muscle that exhibits a low metabolic rate and may help to regulate energy use and promote efficiency in this hard-working and vital organ.

Muscle cells are highly specialized cells that are able to physically contract and produce force. Many variables contribute to the active generation of force, with the availability of calcium in the cell interior playing a major role in the process of muscle contraction. However, recent studies have also implicated the state of a key contractile protein called myosin. Myosin is a motor protein that binds to another contractile protein (called actin) and, using energy it liberated from ATP, pulls on the actin to physically shorten the muscle.

"We have recently identified a new 'super' relaxed state of myosin in resting skeletal muscle, called the SRX," says senior study author, Dr. Roger Cooke from the University of California, San Francisco. "The SRX state has a much smaller ATP turnover rate and shows that "relaxed" myosin comes in at least two states that differ with regards to energy utilization. By analogy with another motor, active myosin generating force is akin to a car racing down the road.

The normal relaxed myosin is similar to a car stopped at a traffic light with the motor running, and the counterpart of the SRX is a car parked beside the road with the motor off. In the current study, we sought to build on our earlier work in skeletal muscle and examine the SRX state in cardiac muscle cells."

Dr. Cooke's group showed that there is an SRX state in resting cardiac muscle cells that is similar to the SRX state in resting skeletal muscle cells.

The researchers went on to show that when you look at active muscle, the SRX state is quite different in cardiac muscle compared to skeletal muscle. "We observed a rapid transition of myosin out of the SRX state in active skeletal muscle cells, while, somewhat surprisingly, the SRX state was maintained in active cardiac muscle cells," says Dr. Cooke. This suggests that the SRX plays a very different role in these different types of muscle.

"We identified a new state of myosin in cardiac muscle with a very low ATP turnover rate that could play a role in decreasing the metabolic load of the myocardium," explains Dr. Cooke. "The mechanism proposed here for cardiac muscle suggests that therapeutic interventions that increase the population of the SRX would be cardio-protective during times of stress. They may also be useful in preserving organs for transplant."

[http://www.eurekalert.org/pub\\_releases/2011-04/chb-iro041811.php](http://www.eurekalert.org/pub_releases/2011-04/chb-iro041811.php)

## **Improved recovery of motor function after stroke**

### ***A combination therapy, including a compound already used by humans, restores skilled use of limb in rodent model***

After the acute treatment window closes, the only effective treatment for stroke is physical/occupational therapy. Now scientists from Children's Hospital Boston report a two-pronged molecular therapy that leads to significant recovery of skilled motor function in a rat model of stroke. Their findings are reported April 20 in the *Journal of Neuroscience*.

By combining two molecular therapies - each known to promote some recovery on its own - the researchers achieved more nerve growth and a greater recovery of motor function than with either treatment alone. One therapy, inosine, is a naturally-present molecule that promotes nerve growth; the other is NEP1-40, an agent that counteracts natural inhibitors of nerve growth. "When you put these two together, you get much stronger growth of new circuits than either one alone, and very striking functional improvements," says senior author Larry Benowitz, PhD, of the Children's Department of Neurosurgery.

Strokes in humans often damage the motor cortex on one side of the brain, interfering with skilled motor functions on the opposite side of the body. Led by Laila Zai, PhD, a postdoctoral fellow in Benowitz's lab and the study's first author, the researchers modeled this scenario by inducing strokes on one side of the rats' brains - specifically in a part of the motor cortex that controls forelimb movement. They then examined the rats' ability to perform a skilled reaching task - retrieving food - with the forelimb on the opposite side.

After 3 to 4 weeks, rats treated with both inosine and NEP1-40 could perform the task - which required coordinated movements of the paw and digits - with success rates equivalent to those before the stroke. Benowitz likens the complexity of this task to a person eating with utensils or operating a joystick.

Benowitz has three issued US patents and several US and foreign patent applications pending for the use of inosine to treat stroke, spinal cord injury and traumatic brain injury, and a pending patent application for the inosine/NEP1-40 combined treatment of CNS injury. Earlier studies from his lab, including one published in 2002 and another published last year, demonstrated that inosine encourages nerve fibers to grow from the uninjured side of the brain into regions of the spinal cord that have lost nerve fibers due to stroke. This compensatory rewiring of neural circuits was matched by functional improvements. A separate 2007 study from the University of Cambridge also found that inosine promotes recovery of skilled motor function following traumatic brain injury in rats.

Inosine works by activating a key regulator of nerve growth (an enzyme known as Mst3b). It has a history of safe usage in humans - it is widely available as a nutritional supplement, and is currently being investigated in clinical trials for the treatment of multiple sclerosis and Parkinson's disease.

NEP1-40 complements inosine's effects by counteracting molecules outside of nerve cells that inhibit nerve growth. Specifically, it blocks signaling through the Nogo receptor, shown by a number of studies to promote the rewiring of neural circuits and to improve functional recovery after stroke.

Benowitz believes circuit rewiring is a promising approach to treating stroke because that is what is thought to underlie the recovery that happens naturally. People with strokes often do regain some function that correlates with shifts in activity to the uninjured parts of the brain. In animal studies, these shifts in brain activity correlate with the growth of new branches from uninjured nerve fibers.

The researchers also found that inosine administered together with environmental enrichment (a model for physical/occupational therapy in humans) led to greater recovery of both nerve growth and motor function. "Physical/occupational therapy should always be part of the strategy," Benowitz says.

*The study was funded by the National Institutes of Health, Alseres Pharmaceuticals and the Dr. Miriam and Sheldon G. Adelson Medical Research Foundation (AMRF).*

[http://www.eurekalert.org/pub\\_releases/2011-04/uok-nrs041911.php](http://www.eurekalert.org/pub_releases/2011-04/uok-nrs041911.php)

## **New research suggests right-handedness prevailed 500,000 years ago**

### ***Right-handedness is a distinctively human characteristic, with right-handers outnumbering lefties nine-to-one. But how far back does right-handedness reach in the human story?***

Researchers have tried to determine the answer by looking at ancient tools, prehistoric art and human bones, but the results have not been definitive.

Now, David Frayer, professor of anthropology at the University of Kansas, has used markings on fossilized front teeth to show that right-handedness goes back more than 500,000 years. He is the lead author (with colleagues in Croatia, Italy and Spain) of a paper published this month in the British journal *Laterality*.

His research shows that distinctive markings on fossilized teeth correlate to the right or left-handedness of individual prehistoric humans.

"The patterns seen on the fossil teeth are directly and consistently produced by right or left hand manipulation in experimental work," Frayer said.

The oldest teeth come from a more than 500,000-year-old chamber known as Sima de los Huesos near Burgos, Spain, containing the remains of humans believed to be ancestors of European Neandertals. Other teeth studied by Frayer come from later Neandertal populations in Europe.

"These marks were produced when a stone tool was accidentally dragged across the labial face in an activity performed at the front of the mouth," said Frayer. "The heavy scoring on some of the teeth indicates the marks were produced over the lifetime of the individual and are not the result of a single cutting episode."

Overall, Frayer and his co-authors found right-handedness in 93.1 percent of individuals sampled from the Sima de los Huesos and European Neandertal sites. "It is difficult to interpret these fossil data in any way other than that laterality was established early in European fossil record and continued through the Neandertals," said Frayer. "This establishes that handedness is found in more than just recent Homo sapiens."

Frayer said that his findings on right-handedness have implications for understanding the language capacity of ancient populations, because language is primarily located on the left side of the brain, which controls the right side of the body, there is a right handedness-language connection. "The general correlation between handedness and brain laterality shows that human brains were lateralized in a 'modern' way by at least half a million years ago and the pattern has not changed since then," he said. "There is no reason to suspect this pattern does not extend deeper into the past and that language has ancient, not recent, roots."

[http://www.eurekalert.org/pub\\_releases/2011-04/uoa-per041911.php](http://www.eurekalert.org/pub_releases/2011-04/uoa-per041911.php)

### **Peppermint earns respect in mainstream medicine**

#### ***University of Adelaide researchers have shown for the first time how peppermint helps to relieve Irritable Bowel Syndrome, which affects up to 20% of the population.***

In a paper published this week in the international journal Pain, researchers from the University's Nerve-Gut Research Laboratory explain how peppermint activates an "anti-pain" channel in the colon, soothing inflammatory pain in the gastrointestinal tract.

Dr Stuart Brierley says while peppermint has been commonly prescribed by naturopaths for many years, there has been no clinical evidence until now to demonstrate why it is so effective in relieving pain.

"Our research shows that peppermint acts through a specific anti-pain channel called TRPM8 to reduce pain sensing fibres, particularly those activated by mustard and chilli. This is potentially the first step in determining a new type of mainstream clinical treatment for Irritable Bowel Syndrome (IBS)," he says.

IBS is a gastrointestinal disorder, causing abdominal pain, bloating, diarrhoea and/or constipation. It affects about 20% of Australians and costs millions of dollars each year in lost productivity, work absenteeism and health care. "This is a debilitating condition and affects many people on a daily basis, particularly women who are twice as likely to experience Irritable Bowel Syndrome," Dr Brierley says.

"Some people find their symptoms appear after consuming fatty and spicy foods, coffee and alcohol, but it is more complex than that. There appears to be a definite link between IBS and a former bout of gastroenteritis, which leaves nerve pain fibres in a heightened state, altering mechanisms in the gut wall and resulting in ongoing pain."

Dr Brierley says the recent floods in Queensland and Victoria could result in a spike of gastroenteritis cases in Australia due to the contamination of some water supplies in affected regions.

He said case studies in Europe and Canada showed that many people who contracted gastroenteritis from contaminated water supplies went on to experience IBS symptoms that persisted for at least eight years.

There is no cure for IBS and it often comes and goes over a person's lifetime. Apart from gastroenteritis and food intolerance, IBS can be brought on by food poisoning, stress, a reaction to antibiotics, and in some cases is genetic. Dr Brierley is one of 25 researchers who work at the University of Adelaide's Nerve-Gut Research Laboratory, hoping to find cures and treatments for a range of intestinal diseases.

[http://www.eurekalert.org/pub\\_releases/2011-04/bmj-saw041911.php](http://www.eurekalert.org/pub_releases/2011-04/bmj-saw041911.php)

### **Study adds weight to link between calcium supplements and heart problems**

#### ***Research: Calcium supplements with or without vitamin D and risk of cardiovascular events: Reanalysis of the Women's Health Initiative limited access dataset and meta-analysis***

New research published on bmj.com today adds to mounting evidence that calcium supplements increase the risk of cardiovascular events, particularly heart attacks, in older women.

The findings suggest that their use in managing osteoporosis should be re-assessed.

Calcium supplements are often prescribed to older (postmenopausal) women to maintain bone health. Sometimes they are combined with vitamin D, but it's still unclear whether taking calcium supplements, with or without vitamin D, can affect the heart.

The Women's Health Initiative (WHI) study - a seven-year trial of over 36,000 women – found no cardiovascular effect of taking combined calcium and vitamin D supplements, but the majority of participants were already taking personal calcium supplements, which may have obscured any adverse effects.

So a team of researchers, led by Professor Ian Reid at the University of Auckland, re-analysed the WHI results to provide the best current estimate of the effects of calcium supplements, with or without vitamin D, on the risk of cardiovascular events. They analysed data from 16,718 women who were not taking personal calcium supplements at the start of the trial and found that those allocated to combined calcium and vitamin D supplements were at an increased risk of cardiovascular events, especially heart attack.

By contrast, in women who were taking personal calcium supplements at the start of the trial, combined calcium and vitamin D supplements did not alter their cardiovascular risk.

The authors suspect that the abrupt change in blood calcium levels after taking a supplement causes the adverse effect, rather than it being related to the total amount of calcium consumed. High blood calcium levels are linked to calcification (hardening) of the arteries, which may also help to explain these results.

Further analyses - adding data from 13 other trials, involving 29,000 people altogether - also found consistent increases in the risk of heart attack and stroke associated with taking calcium supplements, with or without vitamin D, leading the authors to conclude that these data justify a reassessment of the use of calcium supplements in older people. But in an accompanying editorial, Professors Bo Abrahamsen and Opinder Sahota argue that there is insufficient evidence available to support or refute the association.

Because of study limitations, they say "it is not possible to provide reassurance that calcium supplements given with vitamin D do not cause adverse cardiovascular events or to link them with certainty to increased cardiovascular risk. Clearly further studies are needed and the debate remains ongoing."

<http://www.nytimes.com/2011/04/19/health/19mind.html>

## **Come On, I Thought I Knew That!**

By **BENEDICT CAREY**

***Trick question: Is it easier to remember a new fact if it appears in normal type, like this, or in big, bold letters, like this?***

The answer is neither. Font size has no effect on memory, even though most people assume that bigger is better. But font style does. New research finds that people retain significantly more material - whether science, history or language - when they study it in a font that is not only unfamiliar but also hard to read.

Psychologists have long known that people's instincts about how well they've learned a subject are often way off. The feel of a study session can be a poor reflection of its nutritional value: Concepts that seem perfectly clear become fuzzy at exam time, and those that are hard to grasp somehow click into place when it counts.

In recent years, researchers have begun to clarify why this is so, and in some cases how to correct for it. The findings are especially relevant nowadays, experts say.

"So much of the learning that we do now is unsupervised, on our own," said Robert A. Bjork, a psychologist at the University of California, Los Angeles, "that it's crucial to be able to monitor that learning accurately; that is, to know how well we know what we know, so that we avoid fooling ourselves."

Mistakes in judging what we know - in metacognition, as it's known - are partly rooted in simple biases. For instance, most people assume when studying that newly learned facts will long be remembered and that further practice won't make much difference. These beliefs are subconscious and automatic, studies find, even though people know better when they stop to think about it.

Yet overconfidence also develops as a result of the brain's natural tendency to find shortcuts - and to quickly forget that it used them. In a recent report in the journal PNAS, researchers at Harvard and Duke had college students take what they thought was an I.Q. test. Some got an answer key with the test "to check their answers afterward," and others did not.

To no one's surprise, those who got the key peeked at it and did better on the test, on average, than those without it. But after grading their tests, both groups of students predicted how well they would do on a hypothetical longer test without the answer key. Those who had seen the key expected a far higher score on the future test than did those who hadn't.

"The finding was that people who use an answer key when taking a test see their score as a sign of their innate ability, selectively forgetting that the key helped them achieve the score," said the lead author, Zoe Chance, a doctoral student in marketing at Harvard Business School.

Without the answers handy, those confident students did no better on an actual second test than the others.

FAMILIAR FONT USED IN TESTS

**Has brown eyes**

16pt Arial

LESS FAMILIAR FONTS

*Eats flower petals and*

12pt Comic Sans MS (italicized)

*Twelve feet tall, eats green*

12pt Bodoni MT Italic

**The English language is one of**

Haettenschweiler

*History is filled with the*

Monotype Corsiva

Anyone who has ever peeked at the answers at the back of the physics or chemistry textbook already suspects this. It's one thing to study a solution when the problem itself is totally unfamiliar, requiring techniques that haven't yet been learned. It is another to scan the answers when problems are familiar but difficult. Those problem sets go more smoothly, confidence goes up, the temptation to take a study break grows stronger. These sensations reflect more than simple self-deception.

Even hints or answers that are not consciously remembered alter how the brain processes a problem or question, making the experience very different from an unaided exam question. In a 1996 study, researchers at Macalester College and New York University had subjects solve 60 anagrams and rate how difficult each one would be for others to solve. One group of participants had already seen the answers to half of the puzzles in an earlier phase of the study, scattered like so many detective-novel clues in a long list of random words. As a result, they solved those anagrams faster and rated them as significantly easier to solve than the other half - without consciously remembering having seen the answers.

"Studying something in the presence of an answer, whether it's conscious or not, influences how you interpret the question," Dr. Bjork said. "You don't appreciate all of the other things that would have come to mind if the answer weren't there.

"Let's say you're studying capitals and you see that Australia's is Canberra. O.K., that seems easy enough. But when the exam question appears, you think: 'Uh oh, was it Sydney? Melbourne? Adelaide?'"

That's why some experts are leery of students' increasing use of online sites like Cramster, Course Hero, Koofers and others that offer summaries, step-by-step problem solving and copies of previous exams. The extra help may provide a valuable supplement to a difficult or crowded course, but it could also leave students with a false sense of mastery.

Even course outlines provided by a teacher, a textbook or other outside source can create a false sense of security, some research suggests. In one experiment, researchers found that participants studying a difficult chapter on the industrial uses of microbes remembered more when they were given a poor outline - which they had to rework to match the material - than a more accurate one.

One reason for this has to do with a cognitive quality known as fluency, a measure of how easy a piece of information is to process. The brain automatically associates perceptual fluency, or ease of storage, with retrieval fluency, ease of recall. This is a good rule of thumb for lots of new facts: some people are especially good at remembering directions, others are better with names, still others with recipe ingredients, sports statistics, jokes. But it's not as good a guide when studying difficult concepts that don't fall easily into a person's areas of expertise or interest.

"For example, we know that if you study something twice, in spaced sessions, it's harder to process the material the second time, and people think it's counterproductive," said Nate Kornell, a psychologist at Williams College. "But the opposite is true: You learn more, even though it feels harder. Fluency is playing a trick on judgment."

A study to be published this year in the journal *Psychological Science*, led by Dr. Kornell, shows how strong this effect can be. Participants studied a list of words printed in fonts of varying sizes and judged how likely they would be to remember them on a later test. Sure enough, they were most confident that they'd remember the words in large print, rating font size (ease of processing) as more likely to sustain memory even than repeated practice. They got it exactly backward. On real tests, font size made no difference and practice paid off, the study found.

And so it goes, researchers say, with most study sessions: difficulty builds mental muscle, while ease often builds only confidence. At least one group has demonstrated this principle in dramatic fashion, also using fonts.

In a recent study published in the journal *Cognition*, psychologists at Princeton and Indiana University had 28 men and women read about three species of aliens, each of which had seven characteristics, like "has blue eyes," and "eats flower petals and pollen." Half the participants studied the text in 16-point Arial font, and the other half in 12-point Comic Sans MS or 12-point Bodoni MT, both of which are relatively unfamiliar and harder for the brain to process. After a short break, the participants took an exam, and those who had studied in the harder-to-read fonts outperformed the others on the test, 85.5 percent to 72.8 percent, on average.

To test the approach in the classroom, the researchers conducted a large experiment involving 222 students at a public school in Chesterland, Ohio. One group had all its supplementary study materials, in English, history and science courses, reset in an unusual font, like Monotype Corsiva. The others studied as before. After the lessons were completed, the researchers evaluated the classes' relevant tests and found that those students who'd been squinting at the stranger typefaces did significantly better than the others in all the classes - particularly in physics.

“The reason that the unusual fonts are effective is that it causes us to think more deeply about the material,” a co-author of the study, Daniel M. Oppenheimer, a psychologist at Princeton, wrote in an e-mail. “But we are capable of thinking deeply without being subjected to unusual fonts. Think of it this way, you can’t skim material in a hard to read font, so putting text in a hard-to-read font will force you to read more carefully.”

Then again, so will raw effort, he and other researchers said. Concentrating harder. Making outlines from scratch. Working through problem sets without glancing at the answers. And studying with classmates who test one another.

The payoff may go beyond a higher grade. “Students these days are on a treadmill, there’s so much going on in their lives,” Dr. Bjork said. “But monitoring learning is not simply a matter of a higher G.P.A., it’s more efficient - potentially a great savings in time.”

<http://www.newscientist.com/article/mg21028084.600-headset-gives-a-voice-to-the-voice-boxless.html>

### **Headset gives a voice to the voice box-less**

**\* 19 April 2011 by Helen Knight**

#### ***People who have lost their larynx to cancer could speak again, thanks to a device that can interpret facial movements when the wearer mouths a word***

IMAGINE you open your mouth to speak but not a single word emerges. This is the distressing and frustrating situation faced by people who have had their larynx removed following cancer, disease or injury. To help them communicate they are often fitted with a valve in their throat to divert air from the lungs to the oesophagus when they exhale, generating a form of speech. But these valves tend to become clogged after only a few months and need to be replaced.

So a team in the UK is developing a device that can detect and interpret facial movements when someone mouths a word, recognising what they are saying. "We can pick up information about the way they are moving their lips, teeth and tongue around, and from that information reconstruct their speech," says team member Phil Green at the University of Sheffield.

The device uses small magnets placed inside the mouth and on the tongue to create a magnetic field. Changes in the field as the person mouths a word are detected by sensors attached to an external headset.

The system is trained to recognise the patterns of positional changes that correspond to the individual wearer mouthing particular words. So far, the system can recognise about 50 words, says Green.

The team plans to develop magnets that can be safely implanted into the tongue, says team leader James Gilbert at the University of Hull. The researchers are also aiming to reduce the size of the headset that holds the sensors down to that of a Bluetooth device.

Still, it will be a challenge to arrange the magnets in such a way that they produce enough information to recognise what the wearer is saying without causing them discomfort, says Patrick Naylor, an expert in speech recognition and enhancement at Imperial College London.

While losing your speech entirely is thankfully relatively rare, thousands of people each year who suffer a stroke - or those with cerebral palsy, Parkinson's disease or motor neurone disease - can lose the ability to speak coherently. Just as human listeners have trouble understanding impaired speech, so do conventional speech-recognition systems, says Stuart Cunningham, also at the University of Sheffield. He and his colleagues are developing an iPad-sized prototype that could learn to recognise impaired speech and replay a clearer version.

This system is trained on a number of recordings of the person's voice so that it learns to recognise their individual speech patterns. Once the system has recognised a word, it is replayed by a voice synthesiser.

Alternatively, a few minutes of voice recording is taken from a family member - or the person themselves, if made before their impairment becomes too severe- and used to adapt a standard artificial voice. Devices that can clarify impaired speech are far quicker than relying on typed text, says Cunningham.

His team's prototype was developed in collaboration with the National Health Service, communication device maker Toby Churchill and speech-recognition specialist El Pedium Technologies, all in the UK. They plan to begin testing on people in the next 12 months.

#### **Talking with Tara**

AN ANIMATED talking avatar could help people learn a foreign language.

The avatar, named Tara, is designed to show people learning another language the precise mouth movements that should be made to generate a given word. As well as an external view of Tara's speaking head, the system also displays the internal workings of her mouth and tongue as the word is spoken, says its developer Priya Dey, at the University of Sheffield, UK. These were generated from magnetic resonance images taken of Dey's own head and neck as she was speaking.

In a small pilot trial of five native Arabic speakers learning English, Dey found that the talking head helped improve pronunciation more than audio alone. A larger trial will follow.

[http://www.eurekalert.org/pub\\_releases/2011-04/cwru-asc041811.php](http://www.eurekalert.org/pub_releases/2011-04/cwru-asc041811.php)

## **A scratched coating heals itself**

### **Collaboration among Case Western Reserve University, the University of Fribourg and the Army Research Laboratory uses light to trigger repair**

CLEVELAND-Your 6-year-old found a nail in the garage and drew pictures across the side of your new car.

Gnash your teeth now, but researchers at Case Western Reserve University, U.S., say the fix-up may be cheap and easy to do yourself in the not-too-distant future. Together with partners in the USA and Switzerland, they have developed a polymer-based material that can heal itself when placed under ultraviolet light for less than a minute. Their findings are published in the April 21 issue of Nature.

The team involves researchers at Case Western Reserve University in Cleveland (OH) led by Stuart J. Rowan, a team at the Adolphe Merkle Institute of the University of Fribourg led by Christoph Weder, and researchers at the Army Research Laboratory at Aberdeen Proving Ground (MD) led by Rick Beyer.

The scientists envision that re-healable materials like theirs could be used in automotive paints, varnishes for floors and furniture, and many other applications. Their polymers aren't ready for commercial use, they acknowledge, but prove that the concept works. The key?

"These polymers have a Napoleon Complex: in reality they're pretty small but are designed to behave like they're big by taking advantage of specific weak molecular interactions," said Stuart Rowan, a professor of macromolecular engineering and science and Director of the Institute for Advanced Materials at Case Western Reserve University. "Their molecular design allows the materials to change their properties in response to a high dose of ultraviolet light," said Christoph Weder, a professor of polymer chemistry and materials and the director of the Adolphe Merkle Institute.

The new materials were created by a mechanism known as supramolecular assembly. Unlike conventional polymers, which consist of long, chain-like molecules with thousands of atoms, these materials are composed of smaller molecules, which are assembled into longer, polymer-like chains using metal ions as "molecular glue." The result: the new materials, which the scientists call "metallo-supramolecular polymers," behave in many ways like normal polymers.

But when irradiated with intense ultraviolet light, the assembled structures are temporarily unglued. This transforms the originally solid material into a liquid that flows easily. When the light is switched off, the material re-assembles and solidifies again: the original properties are restored. Using lamps such as those dentists use to cure fillings, the researchers repaired scratches in their polymers. Wherever they waved the light beam, the scratches filled up and disappeared, much like a cut that heals and leaves no trace on skin.

Tests showed the researchers could repeatedly scratch and heal their materials in the same location.

"We can simply use heat to heal these materials," Mark Burnworth, a graduate student at Case Western Reserve University, said. "But by using light, we have more control as it allows us to target only the defect and leave the rest of the material untouched."

The researchers systematically investigated several new polymers to find an optimal combination of mechanical properties and healing ability. They found metal ions that drive the assembly process via weaker chemical interactions serve best as the light-switchable molecular glue.

They also found the materials that assembled in the most orderly microstructures had the best mechanical properties. But, healing efficiency improved as structural order decreased.

"Understanding these relationships is critical for allowing us improve the lifetime of coatings tailored to specific applications, like windows in abrasive environments" Beyer said.

According to Rowan, "One of our next steps is to use the concepts we have shown here to design a coating that would be more applicable in an industrial setting."

*The research was funded by the Army Research Office of the US Army Research Laboratory, the US National Science Foundation, and the Adolphe Merkle Foundation.*

*A video about the research can be seen at: <http://www.youtube.com/watch?v=h-fka0wfy8w>*

[http://www.eurekalert.org/pub\\_releases/2011-04/uoca-eoh042011.php](http://www.eurekalert.org/pub_releases/2011-04/uoca-eoh042011.php)

## **Evolution of human 'super-brain' tied to development of bipedalism, tool-making**

### **CU-Boulder archaeologist believes a collective mind of humans developed no later than 75,000 years ago in Africa and fostered language, art and technology**

Scientists seeking to understand the origin of the human mind may want to look to honeybees - not ancestral apes - for at least some of the answers, according to a University of Colorado Boulder archaeologist.

CU-Boulder Research Associate John Hoffecker said there is abundant fossil and archaeological evidence for the evolution of the human mind, including its unique power to create a potentially infinite variety of thoughts expressed in the form of sentences, art and technologies. He attributes the evolving power of the mind

to the formation of what he calls the "super-brain," or collective mind, an event that took place in Africa no later than 75,000 years ago.

An internationally known archaeologist who has worked at sites in Europe and the Arctic, Hoffecker said the formation of the super-brain was a consequence of a rare ability to share complex thoughts among individual brains. Among other creatures on Earth, the honeybee may be the best example of an organism that has mastered the trick of communicating complex information - including maps of food locations and information on potential nest sites from one brain to another - using their intricate "waggle dance."

"Humans obviously evolved a much wider range of communication tools to express their thoughts, the most important being language," said Hoffecker, a fellow at CU's Institute of Arctic and Alpine Research. "Individual human brains within social groups became integrated into a neurologic Internet of sorts, giving birth to the mind."

While anatomical fossil evidence for the capability of speech is controversial, the archaeological discoveries of symbols coincides with a creative explosion in the making of many kinds of artifacts. Abstract designs scratched on mineral pigment show up in Africa about 75,000 years ago and are widely accepted by archaeologists as evidence for symbolism and language. "From this point onward there is a growing variety of new types of artifacts that indicates a thoroughly modern capacity for novelty and invention."

The roots of the mind and the super-brain lie deep in our past and are likely tied to fundamental aspects of our evolution like bipedalism and making stone tools, he said. It was from the making of tools that early humans first developed their ability to project complex thoughts or mental representations outside the individual brain - our own version of the honeybee waggle dance, Hoffecker said.

While crude stone tools crafted by human ancestors beginning about 2.5 million years ago likely were an indirect consequence of bipedalism - which freed up the hands for new functions - the first inklings of a developing super-brain likely began about 1.6 million years ago when early humans began crafting stone hand axes, thought by Hoffecker and others to be one of the first external representations of internal thought.

Ancient hand axes achieved "exalted status" as mental representations since they bear little resemblance to the natural objects they were made from - generally cobbles or rock fragments. "They reflect a design or mental template stored in the nerve cells of the brain and imposed on the rock, and they seemed to have emerged from a strong feedback relationship among the hands, eyes, brains and the tools themselves," he said.

The emerging modern mind in Africa was marked by a three-fold increase in brain size over 3-million-year-old human ancestors like Lucy, thought by some to be the matriarch of modern humans. Humans were producing perforated shell ornaments, polished bone awls and simple geometric designs incised into lumps of red ochre by 75,000 years ago. "With the appearance of symbols and language - and the consequent integration of brains into a super-brain - the human mind seems to have taken off as a potentially unlimited creative force," he said.

The dispersal of modern humans from Africa to Europe some 50,000 to 60,000 years ago provides a "minimum date" for the development of language, Hoffecker speculated. "Since all languages have basically the same structure, it is inconceivable to me that they could have evolved independently at different times and places."

A 2007 study led by Hoffecker and colleagues at the Russian Academy of Sciences pinpointed the earliest evidence of modern humans in Europe dating back 45,000 years ago. Located on the Don River 250 miles south of Moscow, the multiple sites, collectively known as Kostenki, also yielded ancient bone and ivory needles complete with eyelets, showing the inhabitants tailored furs to survive the harsh winters.

The team also discovered a carved piece of mammoth ivory that appears to be the head of a small figurine dating to more than 40,000 years ago. "If that turns out to be the case, it would be the oldest piece of figurative art ever discovered," said Hoffecker, whose research at Kostenki is funded in part by the National Science Foundation.

The finds from Kostenki illustrate the impact of the creative mind of modern humans as they spread out of Africa into places that were sometimes cold and lean in resources, Hoffecker said. "Fresh from the tropics, they adapted to ice age environments in the central plain of Russia through creative innovations in technology."

Ancient musical instruments and figurative art discovered in caves in France and Germany date to before 30,000 years ago, he said. "Humans have the ability to imagine something in the brain that doesn't exist and then create it," he said. "Whether it's a hand axe, a flute or a Chevrolet, humans are continually recombining bits of information into novel forms, and the variations are potentially infinite."

While the concept of a human super-brain is analogous to social insects like bees and ants that collectively behave as a super-organism by gathering, processing and sharing information about their environment, there is one important difference, Hoffecker said. "Human societies are not super-organisms - they are composed of people who are for the most part unrelated, and societies filled with competing individuals and families."



Since the emergence of the modern industrial world beginning roughly 500 years ago, creativity driven by the human super-brain has grown by leaps and bounds, from the invention of mechanical clocks to space shuttles. Powerful artificial intelligence could blur the differences between humans and computers in the coming centuries, he said.

Hoffecker is the author of an upcoming book, titled "Landscape of the Mind: Human Evolution and the Archaeology of Thought," to be published by Columbia University Press in May. For more information on Hoffecker's book visit <http://cup.columbia.edu/book/978-0-231-14704-0/landscape-of-the-mind>.

[http://www.eurekalert.org/pub\\_releases/2011-04/uoc-wyi042011.php](http://www.eurekalert.org/pub_releases/2011-04/uoc-wyi042011.php)

### **What's your intestinal bacteria type?**

#### ***New research shows that an individual's intestinal bacteria flora, regardless of nationality, gender and age, organises itself in certain clusters***

As partners in the international research consortium named MetaHit, scientists from the University of Copenhagen have contributed to show that an individual's intestinal bacteria flora, regardless of nationality, gender and age, organises itself in certain clusters. The cluster of intestinal bacteria flora is hypothesised to have an influence on how we react to both our diet and medicine absorbed through the gastro-intestinal tract. The results have recently been published in the journal Nature.

Most people know about blood types, some also know about tissue types. However, now we may need to consider intestinal bacteria types as well. As part of a large, international research consortium, scientists from the University of Copenhagen have recently contributed to map special "enterotypes", which are three distinctive clusters of bacteria in the human distal gut. Each of these enterotypes reflects a certain balance between various categories of bacteria in the distal gut, and is thought to impact intestinal bacteria digest food leavings, and utilise these for energy delivery to the gut and the whole body energy metabolism, and on how various drugs are absorbed through the gastrointestinal tract. The outcome of the project has recently been reported in the journal Nature's online publication for results that deserve immediate exposure.

"The discovery of enterotypes is expected to influence future research within a number of fields," explains Professor Oluf Borbye Pedersen, professor at Novo Nordisk Foundation Center for Basic Metabolic Research at the Faculty of Health Sciences, the University of Copenhagen, and also one of the lead investigators in the international research consortium MetaHIT, which has conducted the project.

"Our results show that we may have uncovered a new 'biological fingerprint' on the same level as blood types and tissue types. The three enterotypes occur across nationalities and are independent of gender and age. Every enterotype has a certain composition of bacteria that have specific functions, for example energy production from degradation of dietary fibres or formation of certain vitamins. This may potentially affect a number of biological functions – discoveries which at a later stage may be translated into individual diet advice or design of drugs that are adapted to the individual enterotype," Oluf Borbye Pedersen adds.

He underlines that the results published in Nature do not show anything about the precise mechanisms by which the three enterotypes individually affect people that host the bacteria. After further research, more intestinal bacteria clusters will most likely be added to the three enterotypes, which have been identified so far. However, the discovery of their existence gives researchers new opportunities for studying how the about 1.5-kilo gut bacteria, which we all have in our digestive system, affects our health.

*The researchers from MetaHIT, an international EU-supported project, have studied 278 volunteers in total from Denmark, Italy, Spain, France, Japan and USA for the paper in Nature. From Denmark, several scientists have contributed from the Novo Nordisk Foundation Center for Basic Metabolic Research at Faculty of Health Sciences, University of Copenhagen; the Lundbeck Foundations Genomics Center, LuCamp; and from the Center for Biological Sequence Analysis, Institute for System Biology at the Technical University of Denmark.*

[http://www.eurekalert.org/pub\\_releases/2011-04/uab-pwd042011.php](http://www.eurekalert.org/pub_releases/2011-04/uab-pwd042011.php)

### **Primordial weirdness: Did the early universe have 1 dimension?**

#### ***Scientists outline a test for the theory, which, if proven, would address major problems in particle physics***

BUFFALO, N.Y. - Did the early universe have just one spatial dimension?

That's the mind-boggling concept at the heart of a theory that University at Buffalo physicist Dejan Stojkovic and colleagues proposed in 2010. They suggested that the early universe - which exploded from a single point and was very, very small at first - was one-dimensional (like a straight line) before expanding to include two dimensions (like a plane) and then three (like the world in which we live today).

The theory, if valid, would address important problems in particle physics.

Now, in a new paper in Physical Review Letters, Stojkovic and Loyola Marymount University physicist Jonas Mureika describe a test that could prove or disprove the "vanishing dimensions" hypothesis.

Because it takes time for light and other waves to travel to Earth, telescopes peering out into space can, essentially, look back into time as they probe the universe's outer reaches.

Gravitational waves can't exist in one- or two-dimensional space. So Stojkovic and Mureika have reasoned that the Laser Interferometer Space Antenna (LISA), a planned international gravitational observatory, should not detect any gravitational waves emanating from the lower-dimensional epochs of the early universe.

Stojkovic, an assistant professor of physics, says the theory of evolving dimensions represents a radical shift from the way we think about the cosmos - about how our universe came to be.

The core idea is that the dimensionality of space depends on the size of the space we're observing, with smaller spaces associated with fewer dimensions. That means that a fourth dimension will open up - if it hasn't already - as the universe continues to expand. The theory also suggests that space has fewer dimensions at very high energies of the kind associated with the early, post-big bang universe.

If Stojkovic and his colleagues are right, they will be helping to address fundamental problems with the standard model of particle physics, including the following:

- \* The incompatibility between quantum mechanics and general relativity. Quantum mechanics and general relativity are mathematical frameworks that describe the physics of the universe. Quantum mechanics is good at describing the universe at very small scales, while relativity is good at describing the universe at large scales. Currently, the two theories are considered incompatible; but if the universe, at its smallest levels, had fewer dimensions, mathematical discrepancies between the two frameworks would disappear.

- \* The mystery of the universe's accelerating expansion. Physicists have observed that the expansion of the universe is speeding up, and they don't know why. The addition of new dimensions as the universe grows would explain this acceleration. (Stojkovic says a fourth dimension may have already opened at large, cosmological scales.)

- \* The need to alter the mass of the Higgs boson. The standard model of particle physics predicts the existence of an as yet undiscovered elementary particle called the Higgs boson. For equations in the standard model to accurately describe the observed physics of the real world, however, researchers must artificially adjust the mass of the Higgs boson for interactions between particles that take place at high energies. If space has fewer dimensions at high energies, the need for this kind of "tuning" disappears.

"What we're proposing here is a shift in paradigm," Stojkovic said. "Physicists have struggled with the same problems for 10, 20, 30 years, and straight-forward extensions of extensions of the existing ideas are unlikely to solve them." "We have to take into account the possibility that something is systematically wrong with our ideas," he continued. "We need something radical and new, and this is something radical and new."

Because the planned deployment of LISA is still years away, it may be a long time before Stojkovic and his colleagues are able to test their ideas this way.

However, some experimental evidence already points to the possible existence of lower-dimensional space.

Specifically, scientists have observed that the main energy flux of cosmic ray particles with energies exceeding 1 teraelectron volt - the kind of high energy associated with the very early universe - are aligned along a two-dimensional plane. If high energies do correspond with lower-dimensional space, as the "vanishing dimensions" theory proposes, researchers working with the Large Hadron Collider particle accelerator in Europe should see planar scattering at such energies. Stojkovic says the observation of such events would be "a very exciting, independent test of our proposed ideas."

[http://www.eurekalert.org/pub\\_releases/2011-04/tmsh-lcd041311.php](http://www.eurekalert.org/pub_releases/2011-04/tmsh-lcd041311.php)

### **Low carbohydrate diet may reverse kidney failure in people with diabetes**

***Researchers from Mount Sinai School of Medicine have for the first time determined that the ketogenic diet, a specialized high-fat, low carbohydrate diet, may reverse impaired kidney function in people with Type 1 and Type 2 diabetes.***

They also identified a previously unreported panel of genes associated with diabetes-related kidney failure, whose expression was reversed by the diet. The findings were published in the current issue of PLoS ONE.

Charles Mobbs, PhD, Professor of Neuroscience and Geriatrics and Palliative Care Medicine at Mount Sinai School of Medicine, and his research team evaluated mice that were genetically predisposed to have Type 1 or 2 diabetes. The mice were allowed to develop diabetic nephropathy, or kidney failure. Half of the mice were put on the ketogenic diet, while the control group maintained a standard high carbohydrate diet. The researcher founds that after eight weeks, kidney failure was reversed in the mice on the ketogenic diet.

"Our study is the first to show that a dietary intervention alone is enough to reverse this serious complication of diabetes," said Dr. Mobbs. "This finding has significant implications for the tens of thousands of Americans diagnosed with diabetic kidney failure, and possibly other complications, each year."

The ketogenic diet is a low-carbohydrate, moderate protein, and high-fat diet typically used to control seizures in children with epilepsy. Many cells can get their energy from ketones, which are molecules produced when the blood glucose levels are low and blood fat levels are high. When cells use ketones instead of glucose for fuel, glucose is not metabolized. Since high glucose metabolism causes kidney failure in diabetes, researchers hypothesized that the ketogenic diet would block those toxic effects of glucose. Considering the extreme requirements of the diet, it is not a long-term solution in adults. However, Dr. Mobbs' research indicates that exposure to the diet for as little as a month may be sufficient to "reset" the gene expression and pathological process leading to kidney failure.

The researchers also identified a large array of genes expressed during diabetic nephropathy not previously known to play a role in the development of this complication. These genes are associated with kidney failure as a result of the stress on cellular function. The team found that the expression of these genes was also reversed in the mice on the ketogenic diet.

Dr. Mobbs and his team plan to continue to research the impact of the ketogenic diet and the mechanism by which it reverses kidney failure in people with diabetes, and in age-related kidney failure. He believes the ketogenic diet could help treat other neurological diseases and retinopathy, a disease that results in vision loss.

"Knowing how the ketogenic diet reverses nephropathy will help us identify a drug target and subsequent pharmacological interventions that mimic the effect of the diet," said Dr. Mobbs. "We look forward to studying this promising development further."

*This study was funded partly by the National Institutes of Health and by the Juvenile Diabetes Research Foundation.*

[http://www.eurekalert.org/pub\\_releases/2011-04/uosc-urs042011.php](http://www.eurekalert.org/pub_releases/2011-04/uosc-urs042011.php)

### **USC research shows critical role of placenta in brain development** **Groundbreaking study has implications for chronic illness, mental health**

Research at the Keck School of Medicine of the University of Southern California's (USC) Zilkha Neurogenetic Institute shows for the first time that the human placenta plays an active role in synthesizing serotonin, paving the way to new treatment strategies that could mitigate health impacts such as cardiovascular disease and mental illness.

The groundbreaking findings, conducted with researchers from Vanderbilt University as part of a Silvio Conte Center of Excellence grant from the National Institute of Mental Health, offer conclusive evidence that the placenta provides serotonin to the fetal forebrain, not through the mother's blood supply, as theorized for the past 60 years. The research, "A transient placental source of serotonin for the fetal forebrain," will be published in the journal *Nature* on April 21, 2011.

"Our research indicates that the placenta actually synthesizes serotonin, and the serotonin is released from the placenta into the fetal bloodstream where it can reach the fetal brain," said lead author Alexandre Bonnin, Ph.D. "The placenta was seen as a passive organ, but we now know that it has significant synthetic capabilities and has a much more critical role in developmental programming of the fetus than previously thought."

Bonnin's work with Pat Levitt, Ph.D., director of the Zilkha Neurogenetic Institute and corresponding author on the paper, included the invention of a unique technology known as a "placentometer" that monitors substances that pass through the mouse placenta from mother to fetus. This technology can incorporate genetic models of human disease, and could lead to targeted therapies that treat the mother without affecting the fetus, or vice versa.

"The findings by Dr. Bonnin and his collaborators open the door for future studies examining the potential role for targeted interventions in high-risk pregnancies where a perturbed intrauterine environment might negatively impact fetal brain development," said Istvan Seri, professor of pediatrics, Keck School, and director, Center for Fetal and Neonatal Medicine at Children's Hospital Los Angeles. "However, it will take many more basic, translational and clinical trials and many years until we can provide evidence that approaches like this one work."

Serotonin, a neurotransmitter known to affect wellbeing in humans, also has been implicated in brain, cardiac and pancreas development. In the early stages of development, neurons that synthesize serotonin develop in the fetal hindbrain, where heart, respiration and other critical functions reside, eventually building their way up to the forebrain, the home of higher cognition and emotional regulation. The study shows that during this gap between hindbrain and forebrain serotonin development, the placenta is an important source of serotonin to the forebrain – a process that could be affected by the mother's nutrition, since her diet is the only source for the essential amino acid tryptophan.

"An altered capacity of the placenta to make and release serotonin could affect the levels of serotonin in the human forebrain as it does in the mouse," said Levitt. "Developmental programming of the fetal brain can set the stage for adult-onset health impacts including heart disease, diabetes and mental illness."

The research relates to a growing body of evidence that subtle, deleterious effects on the fetus as it develops could lead to a lifetime of chronic mental health problems, including anxiety disorders, learning and emotional disabilities and depression.

"Bonnin's research may be of particular importance for early onset brain disorders, such as autism, Asperger's syndrome and pediatric obsessive-compulsive disorder, where investigators are considering a role for serotonin based on human genetic studies," said Randy Blakely, Ph.D., director of the Vanderbilt Conte Center and a collaborator on the paper.

*Alexandre Bonnin, Nick Goeden, Kevin Chen, Melissa L. Wilson, Jennifer King, Jean C. Shih, Randy D. Blakely, Evan S. Deneris, Pat Levitt. "A transient placental source of serotonin for the fetal forebrain." Nature, April 2011.*

<http://www.scientificamerican.com/article.cfm?id=chimps-give-birth-like-humans>

## **Chimps give birth like humans**

***Humans are not alone in having infants that emerge facing backwards.***

**By Joseph Milton of Nature magazine**

A key feature of human childbirth, long thought to be unique to Homo sapiens - the arrival of the baby facing backwards relative to its mother - has been observed in our closest living relatives, chimpanzees.

The discovery, reported April 19 in Biology Letters, calls into question the argument that backwards-facing babies were an important factor in the evolution of midwifery in humans. Rather than searching for assistance when they go into labour, pregnant chimps seek solitude.

"It's clear from our observations that chimp babies are born facing backwards, but they give birth alone," says lead author Satoshi Hirata, a behavioural biologist at the Great Ape Research Institute of Hayashibara Biochemical Laboratories in Tamano, Japan. "So the reverse orientation is clearly not a necessary condition for the evolution of midwifery."

Remarkably, before Hirata and his colleagues filmed three captive chimpanzees giving birth, nobody had observed chimp parturition at close quarters, and the animal's young were assumed to be born facing forwards, as are those of many other non-human primates. Click here to see one of the team's videos.

Hirata thinks this is probably because the timing of birth is unpredictable, and because pregnant females do not like company when they give birth. "They get very nervous," he says.

### **Close relationship**

The researchers were able to observe the births only because of their very close relationship with the animals they study. "We even sleep in the chimpanzee enclosures every night," says Hirata, "so we could be in the same room as the pregnant females and record the behavior from a very close distance."

Hirata says that, during the births, he and his co-workers had no idea that they were witnessing something so momentous. It was only thanks to a discussion with a human-childbirth researcher that the importance of their observations came to light. "She was very surprised to see the orientation of the baby, so we decided to write a paper about it," Hirata says.

The idea that babies being born backwards - making it difficult for the mother to pick up and nurture the child - may have been instrumental in the evolution of midwifery was first suggested by anthropologists in the 1980s. "But their arguments were not based on clear comparative data from non-human primates," says Hirata. "Now our data have clearly shown that's not the case."

### **Unusual humans**

Wenda Trevathan, a biological anthropologist at New Mexico State University in Las Cruces, was one of the first to suggest that fetal orientation played an important part in the evolution of midwifery. "It's taken 25 years for people to start reporting some observations that help confirm or refute my hypothesis," she says, "so I'm glad that finally we've got some observational data on chimpanzees - it's advancing science."

Trevathan says there are still aspects of human labor that make it "unique, or at least very unusual." "One is the series of rotations that the fetus undergoes as it is born - I'm not sure that's been called into question," she says. "Another is routinely seeking assistance." She adds that the orientation of the human infant still provides a compelling explanation for the evolution of midwifery in humans because "assistance definitely facilitates delivery when the baby comes out in that position."

She also thinks her arguments have often been misinterpreted. "I have never said assistance is a necessity in human childbirth, but rather that it's beneficial." Trevathan thinks that the pertinent question is not why humans have evolved midwifery, but rather why chimps have not.

Although the study does not tackle that question, it certainly helps to quash the outmoded idea that humans are distinct from the rest of the animal kingdom. "In a broad sense I think humans tend to believe we are unique," says Hirata, "but that belief is not based on facts."

*This article is reproduced with permission from the magazine Nature. The article was first published on April 20, 2011.*

### **Attractive Men Have Long... Ring Fingers**

***There are intricate links between male exposure to testosterone in the womb, the development of physical traits and what turns on the opposite sex.***

The longer a man's fourth or ring finger is compared to his index finger, the more likely he is to be judged attractive by women, according to a study released Wednesday. The results, published in the British Royal Society's journal *Biological Sciences*, unveil intricate links between foetal exposure of males to hormones, the development of certain physical traits, and what turns on the opposite sex. It also adds to a growing body of research -- conducted under the banner of evolutionary psychology -- suggesting that the drivers of human behavior are found, more than previously suspected, in "nature" rather than "nurture."

Earlier studies had already shown that the size ratio between the fourth and second fingers, especially of the right hand, is a reliable indicator of the extent a man was exposed to testosterone while still in the womb. The bigger the gap between a longer ring finger and a shorter index, the greater the likely impact of the hormone.

For the new study, scientists led by Camille Ferdenzi of the University of Geneva designed an experiment to find out if women are drawn to the telltale signs of high testosterone levels in men -- a symmetrical face, a deeper voice, a particular body odor -- who have this more "masculine" finger configuration.

More than 80 women university students between 18 and 34 looked at pictures of 49 similarly aged men, and were asked to evaluate them for masculinity and attractiveness. Smaller groups of women listened to recordings of the male voices, and smelled samples of their body odor, taken from cotton pads worn under the arm for 24 hours. "The aim was to understand what makes a man attractive," and whether at least some of those qualities "were in part conditioned by the foetal environment," Ferdenzi said in an interview.

For the visual test, the results were unambiguous. "The longer the ring finger compared to the index -- that is, the greater the exposure to testosterone -- the more attractive the face was rated," she said by phone. "We also found that attractiveness and symmetry in the face are highly correlated." Such a preference might have evolved to boost a female's chances of reproductive success through mating with a more virile partner, she said.

Surprisingly, however, women did not consistently tag the same men as "masculine". Nor did their preferences for voice or odors correspond to the longer ring-finger males. "There wasn't any relation between the 2D-4D" -- 2nd digit, 4th digit -- "ratio and the reactions of the women to odor," Ferdenzi said.

One reason, she speculated, may be that voice and body odor are more dependent on fluctuating levels of adult testosterone than on pre-natal testosterone.

The ring-index finger ratio has also proven to be a useful indicator for gauging the risk of prostate cancer, likewise tied to high levels of testosterone. Research published in December showed that the chances of developing the disease drop by a third in men whose index finger is longer than their ring finger.

Other studies have also found a link between exposure to hormones before birth and the development of other diseases, including breast cancer and osteoarthritis. *Content provided by AFP*

[http://www.eurekalert.org/pub\\_releases/2011-04/uoc-edh042111.php](http://www.eurekalert.org/pub_releases/2011-04/uoc-edh042111.php)

### **EPO doping helps combat cerebral malaria**

***Almost 3.3 billion people, half of the world's population, risk being infected with malaria. Despite having effective means against malaria, the WHO reports 250 million cases of malaria each year and more than 700,000 related deaths.***

Researchers at the University of Copenhagen have now discovered that EPO, the doping drug known from professional cycling, can significantly reduce cerebral malaria related deaths.

When more than 700,000 people die from malaria each year it is due to two grave complications, which the malaria parasites manage to cause before they are eliminated by malaria drugs: Cerebral malaria and serious anemia. These two complications are the cause of almost every malaria-related death, with children between one and five years old being especially vulnerable. Cerebral malaria is responsible for half of all malaria related deaths.

At the University of Copenhagen, the research team Pathogenesis from the Centre for Medical Parasitology (CMP) is working on ways to supplement the current malaria treatment with new medical preparations. The researchers are therefore investigating why these two complications have lethal consequences and how we can prevent this from happening. The researchers have, among other things, discovered that the doping drug EPO reduces cerebral malaria related deaths remarkably among test animals. The team is now working on ways to test this and other treatment strategies.

"EPO is an active molecule in the brain where it can protect the brain cells from damage and disease," explains Doctor Jørgen Kurtzhals, associate professor at the CMP.

EPO is naturally produced in the kidneys from where it sends signals to the bone marrow to produce more red blood corpuscles. But it is also produced in a number of other tissues for example the brain.

"We still do not have a treatment against cerebral malaria and we lack understanding of how the disease emerges, even though the parasite does not cross the blood-brain barrier and remains in the path of blood" says Kurtzhals.

Researchers have found that children with high levels of EPO in their cerebrospinal fluid have less risk of dying from brain malaria. "Our laboratory team has studied whether we can treat mice, which are infected with cerebral malaria, with EPO and the results are striking. The risk of dying drops from 100 percent to nearly 0," says Kurtzhals, who also points out that EPO does not remove the parasite from the blood.

"It is still necessary to treat a malaria infection with the current drugs, but EPO can be part of the treatment because it protects the brain while the malaria drugs kill the parasite."

Doctor Jørgen Kurtzhals and his group are now working behind the microscopes to understand the exact molecular mechanisms, which enable EPO to protect the brain from damage of brain malaria. Other laboratories around the world are now testing EPO on malaria patients.

"We know EPO increases the number of red blood cells and their content of the red protein hemoglobin, and this increases the amount of oxygen that can be transported to the body's tissue and cells. This is the effect some athletes and professional cyclists abuse by increasing the outcome of each breath. But besides this effect, EPO also increases the level of hemoglobin in other cells, and this could be the reason why it protects brain cells against brain malaria," says Kurtzhals

The Pathogenesis team at CMP focuses on how to improve the handling of malaria, while the world awaits an effective vaccine. The group's work ranges from basic research in parasitology and pathogenesis to clinical trials with new drugs.

<http://www.newscientist.com/article/dn20405-immortality-of-all-cancer-cells-exposed-as-a-myth.html>

### **Immortality of all cancer cells exposed as a myth**

\* 15:01 21 April 2011 by Andy Coghlan

***Far from being immortal, most cancer cells seem unable to multiply limitlessly and spread throughout the body.***

Dot Bennett of St George's University of London and colleagues found that only four of 37 skin cancer samples they examined displayed the supposed hallmark of cancer. "We thought they'd all be immortal, but they weren't," she says.

By studying the molecular profiles of the cancer cells as they grew in the lab, the team found that many appeared to have hit a "telomere crisis" and stopped dividing. Telomeres are the caps that protect the ends of chromosomes and they shorten every time a cell divides. In a telomere crisis, the tips become so short that the cell mistakes them for DNA breaks and tries to repair them, generating freak cells that die or become dormant.

The team found that the few cancer cells that are immortal activate telomerase reverse transcriptase (TERT), a part of the telomerase enzyme that rebuilds telomeres so they avoid a telomere crisis.

Normally, TERT is active only in sperm or egg cells, so looking for it in a tumour could tell doctors whether the cells are immortal and more likely to spread, helping them decide on the best treatment.

#### **Cancer vaccine**

Last week, Cancer Research UK launched a trial to stop pancreatic cancer spreading with a vaccine composed of fragments of TERT. The body's immune system would recognise the TERT as foreign and mobilise to attack it, bringing all pancreatic cancer cells with active TERT into the firing line too.

A vaccine that acts in a similar way against acute myelogenous leukaemia is being tested by Geron of Menlo Park, California, which has been developing anti-cancer treatments based on telomerase for some time.

Geron also has two major trials under way in breast cancer and non-small cell lung cancer to test imetelstat, a drug that blocks the activity of TERT.

Journal reference: *Pigment Cell & Melanoma Research* (DOI: 10.1111/j.1755-148X.2011.00850.x).

<http://www.physorg.com/news/2011-04-breakthrough-holy-grail-storage.html>

### **Breakthrough in the search for the holy grail for data storage**

***(PhysOrg.com) -- One of The University of Nottingham's leading young scientists has created a new compound which could lead to a breakthrough in the search for high performance computing techniques.***

Dr Steve Liddle, an expert in molecular depleted uranium chemistry, has created a new molecule containing two Uranium atoms which, if kept at a very low temperature, will maintain its magnetism. This type of single-

molecule magnet (SMM) has the potential to increase data storage capacity by many hundreds, even thousands of times - as a result huge volumes of data could be stored in tiny places.

Dr Liddle, a Royal Society University Research Fellow and Reader in the School of Chemistry, has received numerous accolades for his ground breaking research. His latest discovery has just been published in the journal Nature Chemistry.

Dr Liddle said: "This work is exciting because it suggests a new way of generating SMM behaviour and it shines a light on poorly understood uranium phenomena. It could help point the way to making scientific advances with more technologically amenable metals such as the lanthanides. The challenge now is to see if we can build bigger clusters to improve the blocking temperatures and apply this more generally.

Computer hard discs are made up of magnetic material which record digital signals. The smaller you can make these tiny magnets the more information you can store.

Although it may have somewhat negative PR it seems depleted Uranium - a by-product from uranium enrichment and of no use in nuclear applications because the radioactive component has been removed - could now hold some of the key to their research. Dr Liddle has shown that by linking more than one uranium atom together via a bridging toluene molecule SMM behaviour is exhibited.

He said: "At this stage it is too early to say where this research might lead but single-molecule magnets have been the subject of intense study because of their potential applications to make a step change in data storage capacity and realise high performance computing techniques such as quantum information processing and spintronics."

Dr Liddle said: "The inherent properties of uranium place it between popularly researched transition and lanthanide metals and this means it has the best of both worlds. It is therefore an attractive candidate for SMM chemistry, but this has never been realised in polymetallic systems which is necessary to make them work at room temperature." Dr Liddle is a regular contributor to the School of Chemistry's award winning Periodic Table of Videos - periodicvideos.com. The website, created by Brady Haran, the University's film maker in residence, won the 2008 IChemE Petronas Award for excellence in education and training.

*More information: A delocalized arene-bridged diuranium single-molecule magnet, Nature Chemistry (2011)  
doi:10.1038/nchem.1028*

#### Abstract

Single-molecule magnets (SMMs) are compounds that, below a blocking temperature, exhibit stable magnetization purely of molecular origin, and not caused by long-range ordering of magnetic moments in the bulk. They thus show promise for applications such as data storage of ultra-high density. The stability of the magnetization increases with increasing ground-state spin and magnetic anisotropy. Transition-metal SMMs typically possess high-spin ground states, but insufficient magnetic anisotropies. Lanthanide SMMs exhibit large magnetic anisotropies, but building high-spin ground states is difficult because they tend to form ionic bonds that limit magnetic exchange coupling. In contrast, the significant covalent bonding and large spin-orbit contributions associated with uranium are particularly attractive for the development of improved SMMs. Here we report a delocalized arene-bridged diuranium SMM. This study demonstrates that arene-bridged polyuranium clusters can exhibit SMM behaviour without relying on the superexchange coupling of spins. This approach may lead to increased blocking temperatures. *Provided by University of Nottingham*

<http://medicalxpress.com/news/2011-04-israeli-artificial-device-capable-cancer.html>

**Israeli engineers build artificial device capable of detecting cancer in breath (PhysOrg.com) -- Professor Hossam Haick of the Israel Institute of Technology, at Technion, and his team have built an artificial nose which is capable of detecting molecules in human breath that signal the presence of head and neck cancers in people.**

In a paper published in the British Journal of Cancer, Haick describes how he and his colleagues set to work on coming up with a device that could mimic the ability that dogs have demonstrated in detecting certain types of cancers. Such a device is critical for the millions of cancer victims the world over, as head and neck cancers are notoriously difficult to detect until they've reached an advanced stage when they are difficult to treat.

Called the Nanoscale Artificial Nose (NA-NOSE), by its developers, the device consists of five gold nanoparticle sensors and some imaginative software that is able to pick out and detect the patterns of molecules that exist in the breath of people with head, neck or even lung cancer. The sensors are so small, just a few of the molecules they're looking for can change the electrical properties of the materials, signaling a result, which means that they are capable of detecting very low concentrations of such compounds, which is critical due to the fact that human breath is 80% water vapor.

The NA-NOSE was tested using 80 volunteers, most of whom had various head and neck cancers, such as those of the mouth, lips, sinuses, larynx or salivary glands. Head and neck cancers comprise the eighth most common kind worldwide, and in some countries, such as the US, they can account for up to 5% of all cancer cases reported. Also included in the test were some patients with lung cancer. The NA-NOSE was able to

discern the difference between patients with head and neck cancers versus those that were cancer free, between those who had head and neck cancers versus those who had lung cancer and between those who had lung cancer compared to those who were cancer free.

While the results of the test were clearly remarkable, the NA-NOSE still needs to go through much more rigorous testing before it will be deemed suitable for use as an actual diagnosis tool in doctor's offices around the world, but as Haick notes, so far, the results are very promising.

*More information: Diagnosis of head-and-neck cancer from exhaled breath, British Journal of Cancer advance online publication 19 April 2011; doi: 10.1038/bjc.2011.128*

### Abstract

**background:** Head-and-neck cancer (HNC) is the eighth most common malignancy worldwide. It is often diagnosed late due to a lack of screening methods and overall cure is achieved in <50% of patients. Head-and-neck cancer sufferers often develop a second primary tumour that can affect the entire aero-digestive tract, mostly HNC or lung cancer (LC), making lifelong follow-up necessary.

**methods:** Alveolar breath was collected from 87 volunteers (HNC and LC patients and healthy controls) in a cross-sectional clinical trial. The discriminative power of a tailor-made Nanoscale Artificial Nose (NA-NOSE) based on an array of five gold nanoparticle sensors was tested, using 62 breath samples. The NA-NOSE signals were analysed to detect statistically significant differences between the sub-populations using (i) principal component analysis with ANOVA and Student's t-test and (ii) support vector machines and cross-validation. The identification of NA-NOSE patterns was supported by comparative analysis of the chemical composition of the breath through gas chromatography in conjunction with mass spectrometry (GC-MS), using 40 breath samples.

**results:** The NA-NOSE could clearly distinguish between (i) HNC patients and healthy controls, (ii) LC patients and healthy controls, and (iii) HNC and LC patients. The GC-MS analysis showed statistically significant differences in the chemical composition of the breath of the three groups.

**conclusion:** The presented results could lead to the development of a cost-effective, fast, and reliable method for the differential diagnosis of HNC that is based on breath testing with an NA-NOSE, with a future potential as screening tool.

© 2010 PhysOrg.com

[http://www.eurekalert.org/pub\\_releases/2011-04/uoc--omw042111.php](http://www.eurekalert.org/pub_releases/2011-04/uoc--omw042111.php)

### **Optical microscope without lenses produces high-resolution 3-D images on a chip UCLA researchers have redefined the concept of a microscope by removing the lens to create a system that is small enough to fit in the palm of a hand but powerful enough to create three-dimensional tomographic images of miniscule samples.**

The advance, featured this week in the early online edition of the journal Proceedings of the National Academy of Sciences, represents the first demonstration of lens-free optical tomographic imaging on a chip, a technique capable of producing high-resolution 3-D images of large volumes of microscopic objects.

"This research clearly shows the potential of lens-free computational microscopy," said Aydogan Ozcan, senior author of the research and an associate professor of electrical engineering at UCLA's Henry Samueli School of Engineering and Applied Science. "Wonderful progress has been made in recent years to miniaturize life-sciences tools with microfluidic and lab-on-a-chip technologies, but until now optical microscopy has not kept pace with the miniaturization trend."

An optical imaging system small enough to fit onto an opto-electronic chip provides a variety of benefits. Because of the automation involved in on-chip systems, scientific work could be sped up significantly, which might have a great impact in the fields of cell and developmental biology. In addition, the small size not only has great potential for miniaturizing systems but also leads to cost savings on equipment.

The optical microscope, invented more than 400 years ago, has tended to grow larger and more complex as it has been modified to image ever-smaller objects with better resolution. To address this lack of progress in miniaturization, Ozcan's research group - with graduate student Serhan Isikman and postdoctoral scholar Waheb Bishara as lead researchers - developed the new tomographic microscopy platform through the next evolution of a lens-free imaging technology the group created and has been improving for years.

Ozcan, a researcher at the California NanoSystems Institute at UCLA, makes the analogy that a traditional optical microscope is like a huge set of pipes delivering content, in the form of images, to the user. Over years of development, bottlenecks occur that impede further improvement. Even if one part of the system - that is, one bottleneck - is improved, other bottlenecks keep that improvement from being fully realized. Not so with the lens-free system, according to Ozcan.

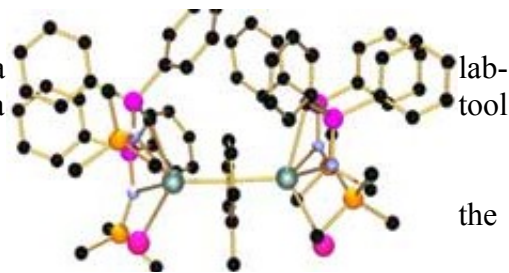
"Lens-free imaging removes the pipes altogether by utilizing an entirely new design," he said.

The system takes advantage of the fact that organic structures, such as cells, are partially transparent. So by shining a light on a sample of cells, the shadows created reveal not only the cells' outlines but details about their sub-cellular structures as well.



"These details can be captured and analyzed if the shadow is directed onto a digital sensor array," Isikman said. "The end result of this process is an image taken without using a lens."

Ozcan envisions this lens-free imaging system as one component in a on-a-chip platform. It could potentially fit beneath a microfluidic chip, a for the precise control and manipulation of sub-millimeter biological samples and fluids, and the two tools would operate in tandem, with the microfluidic chip depositing and subsequently removing a sample from lens-free imager in an automated, or high-throughput, process.



The platform's 3-D images are created by rotating the light source to illuminate the samples from multiple angles. These multiple angles also allow the system to utilize tomography, a powerful imaging technique. Through the use of tomography, the system is able to produce 3-D images without sacrificing resolution.

"The field of view of lens-based microscopes is limited because the lens focuses on a narrow area of a sample," Bishara said. "A lens-free microscope has both a much larger field of view and depth of field because the imaging is done by the digital sensor array and is not constrained by a lens."

*The research was funded by grants from the National Science Foundation, the U.S. Office of Naval Research and the National Institutes of Health and was also supported by the Gates Foundation and the Vodafone Americas Foundation. For more information on the Ozcan research group, visit <http://innovate.ee.ucla.edu/>.*

<http://www.scientificamerican.com/article.cfm?id=ozone-hole-dominates-shifting->

### **Ozone hole dominates shifting Southern Hemisphere climate**

***Climate policymakers and scientists need to look beyond global warming emissions of carbon dioxide and take the loss of stratospheric ozone into account, researchers said on Thursday.***

**By Deborah Zabarenko, Environment Correspondent**

WASHINGTON (Reuters) - Climate policymakers and scientists need to look beyond global warming emissions of carbon dioxide and take the loss of stratospheric ozone into account, researchers said on Thursday.

The stratospheric ozone layer, which shields Earth from solar ultra-violet radiation, has thinned over the South Pole over the last half-century.

This depletion of ozone has shifted the Southern Hemisphere's climate so that dry areas in the subtropics now see about 10 percent more precipitation in summer than they used to, scientists reported in the journal *Science*.

"Ozone is now widely believed to be the dominant agent of climate change in the Southern Hemisphere, so this actually means that the international agreements regulating climate change cannot be confined to dealing with carbon dioxide," said the study's lead author, Sarah Kang of Columbia University.

"They also need to consider ozone," Kang said by telephone.

Carbon dioxide emissions from natural and human-made sources, notably the burning of fossil fuels, is the most frequently cited target of policymakers aiming to curb climate change caused by humans.

However, the depletion of ozone in the atmosphere due largely to commercial and industrial use of chemicals containing chlorofluorocarbons has a powerful impact on large swaths of the Southern Hemisphere, the researchers found.

#### **Winds Shift Toward South Pole**

The stratospheric ozone layer typically absorbs ultra-violet radiation, warming the air below. With the opening of the ozone hole over the South Pole due to chlorofluorocarbon pollution, there was severe cooling instead of warming, which eventually caused a southern shift in the winds that whip from west to east around Antarctica. As this band of winds moved toward the pole, a corresponding dry belt in the subtropics also moved southward, the researchers showed. This left room nearer the equator for a band of increased summer precipitation.

Most of this change is driven by the ozone hole, with a smaller contribution from increased concentration of greenhouse gases in the atmosphere, the study found.

Earlier this month, the United Nations World Meteorological Organization reported record loss of the protective ozone layer over the Arctic, which unlike that in the Antarctic, is not an annual occurrence.

The 40 percent loss of ozone over the Arctic came despite the "very successful" 1987 Montreal Protocol aimed at cutting production and consumption of ozone-destroying chemicals including chlorofluorocarbons and halons, WMO said on April 5.

The substances were once present in refrigerators, spray cans and fire extinguishers, but have been phased out. However, they can linger for decades in the atmosphere, so it will take several decades more before their concentrations drop to pre-1980 levels, WMO said. *(Editing by Cynthia Osterman)*

<http://medicalxpress.com/news/2011-04-vengeance-compound-treatment-painful-adult.html>

## **Back with a vengeance: Compound offers new hope for treatment of painful adult shingles**

### ***UGA compound offers new hope for treatment of painful adult shingles***

Researchers at the University of Georgia and Yale University have discovered a compound with the potential to be more effective than existing agents in treating the very painful blisters known as shingles -- a condition that affects up to 30 percent of Americans, mostly elderly, and for which no specific treatment exists.

Most adults remember the fever, itchy blisters and possibly tiny scars they experienced as children when they had chickenpox, which is caused by the varicella-zoster virus, or VZV. Unfortunately, that memory can come back - with a vengeance - when they are older. The VZV virus from childhood chickenpox hides in the nerves, emerging most frequently in adults over the age of 60 as a blistering rash on one side of the body. The rate of complications, including nerve pain that can persist for months or years after the shingles attack is gone, also increases with age.

The novel and effective anti-shingles agent called L-BHDA may change that. Rights to the shingles treatment have been licensed to Bukwang Pharmaceutical Company for preclinical investigations by the University of Georgia Research Foundation, Inc. and Yale University.

"We need new options for medications with increased potency and specificity that can treat VZV, including strains that may be resistant to existing drugs," said medicinal chemist Chung (David) Chu, Distinguished Research Professor of Pharmaceutical and Biomedical Sciences at UGA, one of the inventors of L-BHDA.

A collaboration between Chu and co-inventor Yung-Chi (Tommy) Cheng, the Henry Bronson Professor of Pharmacology at Yale, has resulted in an extensive portfolio of antiviral compounds that target such diseases as HIV, shingles, hepatitis and cancers.

Chu, who is head of the Drug Discovery Group in the UGA College of Pharmacy, said that although there are generic antiviral drugs to reduce the duration and pain of shingles, and a variety of pain medications and topical creams to relieve long-term pain, "They are only moderately effective. We need more effective anti-VZV agents.

"L-BHDA has the potential to be more effective than existing agents," said Chu. He noted that the new compound has been tested in the laboratory and demonstrated in mice models by a group of researchers headed by Jennifer Moffat, associate professor of microbiology and immunology, State University of New York Upstate Medical University.

A vaccine to prevent shingles, available to older adults since 2006, can cut the likelihood of a shingles attack in half. However, according to a recent study in the American Journal of Preventive Medicine, only a small percentage of older people receive the shot, principally because of cost, lack of insurance reimbursement and shortage of supply.

It is likely that immunization against chickenpox during childhood also protects against shingles, because the vaccine uses a weakened strain of the virus. However, the vaccine was only introduced in 1995, and there are not enough data to provide a definitive answer.

"Dr. Chu and Dr. Cheng have been working diligently to fill a much needed gap in the treatment options for such a prevalent disease," said Rachael Widener, UGARF technology licensing manager. "Before the chicken pox vaccine became widely used in the mid-1990s, older, unvaccinated individuals would have their immunity boosted naturally.

"Now, with less exposure to chicken pox, shingles is becoming more prevalent," said Widener. "This, combined with the aging baby boomer population, underscores the need for more directed treatment. We are hopeful that L-BHDA will allow patients to get well sooner and feel less pain, and will lessen their chances of complications." *Provided by University of Georgia*

<http://www.physorg.com/news/2011-04-ice-lake-mars-bowl.html>

### **Dry ice lake suggests Mars once had a 'Dust Bowl' (Update)**

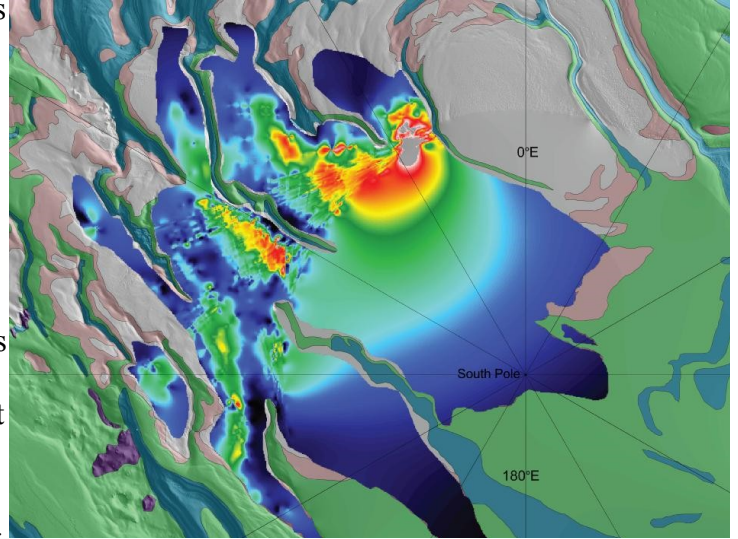
**(PhysOrg.com) -- NASA's Mars Reconnaissance Orbiter has discovered the total amount of atmosphere on Mars changes dramatically as the tilt of the planet's axis varies.**

This process can affect the stability of liquid water, if it exists on the Martian surface, and increase the frequency and severity of Martian dust storms.

Researchers using the orbiter's ground-penetrating radar identified a large, buried deposit of frozen carbon dioxide, or dry ice, at the Red Planet's south pole. The scientists suspect that much of this carbon dioxide enters the planet's atmosphere and swells the atmosphere's mass when Mars' tilt increases. The findings are published in this week's issue of the journal Science.

The newly found deposit has a volume similar to Lake Superior's nearly 3,000 cubic miles (about 12,000 cubic kilometers). The deposit holds up to 80 percent as much carbon dioxide as today's Martian atmosphere. Collapse pits caused by dry ice sublimation and other clues suggest the deposit is in a dissipating phase, adding gas to the atmosphere each year. Mars' atmosphere is about 95 percent carbon dioxide, in contrast to Earth's much thicker atmosphere, which is less than .04 percent carbon dioxide.

"We already knew there is a small perennial cap of carbon-dioxide ice on top of the water ice there, but this buried deposit has about 30 times more dry ice than previously estimated," said Roger Phillips of Southwest Research Institute in Boulder, Colo. Phillips is deputy team leader for the Mars Reconnaissance Orbiter's Shallow Radar instrument and lead author of the report.

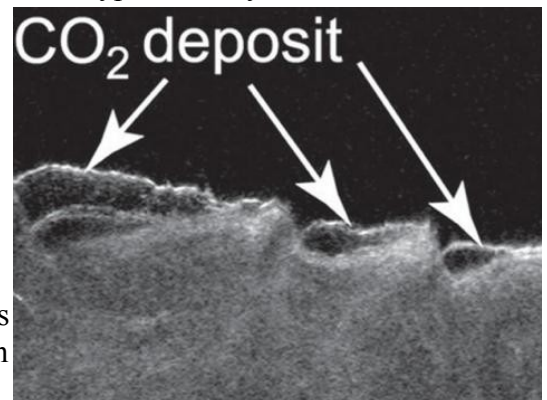


***A newly found, buried deposit of frozen carbon dioxide -- dry ice -- near the south pole of Mars contains about 30 times more carbon dioxide than previously estimated to be frozen near the pole. Image credit: NASA/JPL-Caltech/Sapienza University of Rome/Southwest Research Institute***

"We identified the deposit as dry ice by determining the radar signature fit the radio-wave transmission characteristics of frozen carbon dioxide far better than the characteristics of frozen water," said Roberto Seu of Sapienza University of Rome, team leader for the Shallow Radar and a co-author of the new report. Additional evidence came from correlating the deposit to visible sublimation features typical of dry ice.

"When you include this buried deposit, Martian carbon dioxide right now is roughly half frozen and half in the atmosphere, but at other times it can be nearly all frozen or nearly all in the atmosphere," Phillips said.

An occasional increase in the atmosphere would strengthen winds, lofting more dust and leading to more frequent and more intense dust storms. Another result is an expanded area on the planet's surface where liquid water could persist without boiling. Modeling based on known variation in the tilt of Mars' axis suggests several-fold changes in the total mass of the planet's atmosphere can happen on time frames of 100,000 years or less.



***This cross-section view of underground layers near Mars' south pole is a radargram based on data from the Shallow Subsurface Radar (SHARAD) instrument on NASA's Mars Reconnaissance Orbiter. Researchers interpret the zone that is nearly free of radio-wave reflections (hence dark in the radargram) to be composed of frozen carbon dioxide, or "dry ice." The newly found deposit of dry ice contains enough carbon dioxide to dramatically increase the total amount of atmosphere on Mars when the frozen carbon dioxide vaporizes, as climate models suggest it does at times when the planet's tilt increases. Mars' current atmosphere is about 95 percent carbon dioxide, and this deposit contains up to about 80 percent as much carbon dioxide as the atmosphere does. This cross section covers a transect about 330 kilometers (205 miles) long in a region from about 86 degrees to 87 degrees south latitude and 280 degrees to 10 degrees east longitude. The vertical dimension of the graphic is time delay of the radar echoes. The depth of the tallest portion of the cross section corresponds to about 20 microseconds difference in time delay, which can be converted to roughly 1.7 kilometers (about 1 mile). SHARAD was provided by the Italian Space Agency. Its operations are led by Sapienza University of Rome, and its data are analyzed by a joint U.S.-Italian science team. NASA's Jet Propulsion Laboratory, a division of the California Institute of Technology in Pasadena, manages the Mars Reconnaissance Orbiter for the NASA Science Mission Directorate, Washington. Lockheed Martin Space Systems, Denver, built the spacecraft. Image credit: NASA/JPL-Caltech/Sapienza University of Rome/Southwest Research Institute***

The changes in atmospheric density caused by the carbon-dioxide increase also would amplify some effects of the changes caused by the tilt. Researchers plugged the mass of the buried carbon-dioxide deposit into climate models for the period when Mars' tilt and orbital properties maximize the amount of summer sunshine hitting the south pole. They found at such times, global, year-round average air pressure is approximately 75 percent greater than the current level.

"A tilted Mars with a thicker carbon-dioxide atmosphere causes a greenhouse effect that tries to warm the Martian surface, while thicker and longer-lived polar ice caps try to cool it," said co-author Robert Haberle, a planetary scientist at NASA's Ames Research Center in Moffett Field, Calif. "Our simulations show the polar

caps cool more than the greenhouse warms. Unlike Earth, which has a thick, moist atmosphere that produces a strong greenhouse effect, Mars' atmosphere is too thin and dry to produce as strong a greenhouse effect as Earth's, even when you double its carbon-dioxide content."

The Shallow Radar, one of the Mars Reconnaissance Orbiter's six instruments, was provided by the Italian Space Agency, and its operations are led by the Department of Information Engineering, Electronics and Telecommunications at Sapienza University of Rome. NASA's Jet Propulsion Laboratory, a division of the California Institute of Technology in Pasadena, manages the Mars Reconnaissance Orbiter project for NASA's Science Mission Directorate at the agency's headquarters in Washington. Lockheed Martin Space Systems in Denver built the spacecraft. *Provided by NASA*

[http://www.eurekalert.org/pub\\_releases/2011-04/ats-nat041911.php](http://www.eurekalert.org/pub_releases/2011-04/ats-nat041911.php)

### **New approach to defeating flu shows promise**

***New research on mice has shown that pulmonary administration of granulocyte macrophage-colony stimulating factor (GM-CSF) significantly reduces flu symptoms and prevents death after a lethal dose influenza virus.***

While GM-SCF therapy for humans as a flu prophylaxis or treatment may be years away, the study results were striking: All of the mice treated with GM-SCF survived after being infected with the influenza virus, whereas untreated mice all died from the same infection.

"Such unique and unambiguous results demonstrate the great potential of GM-CSF and may be the remedy for a critical public health priority: developing strategies to reduce the morbidity and mortality from influenza," said Homayoun Shams, PhD, principal investigator of the study. The results were posted online ahead of the print edition of the American Journal of Respiratory and Critical Care Medicine.

Each year, flu infects 3 to 5 million people worldwide and is responsible for 250-500,000 deaths, according to the World Health Organization. Genetic mutations of influenza virus reduce the potency of flu vaccines, and a vaccinated person may contract flu, develop complications and even die due to poor host immune responses to vaccine or mutated virus strains.

Vaccinations work by activating the host's adaptive immunity in advance of infection. However, if the immune system is compromised, a vaccination may not provoke an adequate immune response to confer protection. Additionally, vaccine-induced immunity takes time to develop. If an individual is exposed shortly before or after being vaccinated, the vaccine will likely have little or no effect on his or her immunity.

"Improved methods to protect against influenza are sorely needed, particularly in the face of an impending pandemic. Development of such methods hinges on understanding host mechanisms that confer robust protection against influenza," said Dr. Shams. "Despite the widespread use of vaccines, influenza causes significant morbidity and mortality throughout the world, and those with poor immune systems are particularly more susceptible - such as very young, elderly or immunocompromised individuals."

GM-SCF boosts innate immunity to make it immediately effective against the virus, and its protective effect has not been shown to be strain dependant so far. Alveolar macrophages (AM), which are enhanced by GM-SCF, are an essential piece of the innate immune response and are known to contribute to host defense against flu infections in animal models. "Unlike a vaccine, GM-SCF does not rely heavily on the body's ability to mount an immune counter-attack against a specific antigen or virus strain, but enhances the speed of local responses to virus infection and delicately balances the host immune responses," explained Dr. Shams.

Dr. Shams and colleagues wanted to test the idea that boosting AM by introducing GM-SCF would protect against flu. They used three types of mice to test their hypothesis: wild-type (WT) mice, transgenic mice that do not express any GM-SCF (GM-/-), and transgenic mice that express GM-SCF only in the lung (SPC-GM). They infected all three strains of mice with lethal doses of influenza virus. After progressive weight loss, all WT and GM-/- mice died within days. In contrast, all SPC-GM mice survived, and they gained back the weight they initially lost after a short period.

"This proves the concept that GM-SCF, only in the lung, is sufficient to provide complete protection against infection with otherwise lethal doses of influenza virus strains," said Dr. Shams. "This finding delineates a novel means of conferring marked resistance to influenza through enhancing innate immune mechanisms that depend on AM. We found that SPC-GM mice that overexpress GM-SCF only in the lungs are highly resistant to infection with laboratory and clinical influenza strains, including the recent pandemic swine H1N1 strain."

GM-SCF is already in use in humans as a therapy for neutropenia, and Dr. Shams hopes to eventually test its effectiveness in clinical trials for preventing or treating flu exposure. "If additional work determines that delivery of GM-SCF to the lungs after onset of symptoms improves the outcome of influenza infection, this strategy has great potential to represent a new intervention to reduce morbidity and mortality from influenza in humans," he said.

<http://news.discovery.com/space/spacex-elon-musk-mars-astronauts-20-years-110423.html>

## SpaceX Aims to Put Man on Mars in 10-20 Years

**Elon Musk has announced a time-scale for his company's planetary exploration goals.**

Private US company SpaceX hopes to put an astronaut on Mars within 10 to 20 years, the head of the firm said.

"We'll probably put a first man in space in about three years," Elon Musk told the Wall Street Journal Saturday. "We're going all the way to Mars, I think... best case 10 years, worst case 15 to 20 years."

SpaceX is one of the two leading private space companies in the United States and has won \$75 million from the US space agency NASA to help its pursuit of developing a spacecraft to replace the space shuttle.

The California-based company last year completed its first successful test of an unmanned space capsule into orbit and back. "Our goal is to facilitate the transfer of people and cargo to other planets, and then it will be up to people if they want to go," said Musk, who also runs the Tesla company which develops electric cars.

The US space shuttle program is winding down later this year with final flights of Endeavour set for next week and Atlantis in June, ending an era of American spaceflight that began with the first space shuttle mission in 1981. When the shuttle program ends, the United States hopes private industry will be able to fill the gap by creating the next generation of spacecraft to transport astronauts into space.

"A future where humanity is out there exploring stars is an incredibly exciting future, and inspiring, and that's what we're trying to help make happen," Musk added in the interview.

Earlier this month SpaceX unveiled what Musk has called the world's most powerful rocket, the Falcon Heavy, which will have its first demonstration flight at the end of 2012.

The launcher is designed to lift into orbit satellites or spacecraft weighing more than 53 metric tons, or 117,000 pounds -- more than twice the capacity of the Space Shuttle or Delta IV Heavy launcher.

SpaceX, short for Space Exploration Technologies Corporation, is one of two private companies that NASA has contracted to transport cargo to the International Space Station.

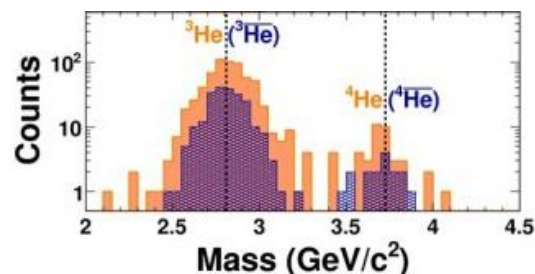
Musk, a South African who made his fortune in the Internet, created SpaceX in 2002.

[http://www.eurekalert.org/pub\\_releases/2011-04/dnl-rpn042211.php](http://www.eurekalert.org/pub_releases/2011-04/dnl-rpn042211.php)

## RHIC Physicists Nab New Record for Heaviest Antimatter

**Newly discovered antihelium-4 could be heaviest stable antinucleus detectable for decades to come**

UPTON, NY -- Members of the international STAR collaboration at the Relativistic Heavy Ion Collider -- a particle accelerator used to recreate and study conditions of the early universe at the U.S. Department of Energy's Brookhaven National Laboratory -- have detected the antimatter partner of the helium nucleus: antihelium-4. This new particle, also known as the anti-alpha, is the heaviest antinucleus ever detected, topping a discovery announced by the same collaboration just last year\*.



*This graph plots particle counts by mass, showing ordinary helium nuclei (He-3 and He-4) in orange, and their antimatter counterparts (antihelium-3 and antihelium-4) in blue. The plot illustrates that the newly discovered antimatter nuclei, antihelium-4, are very cleanly separated from the lighter isotopes, and are at the correct mass.*

Credit: Brookhaven National Laboratory

The new record will likely stand far longer, the scientists say, because the next weightier antimatter nucleus that does not undergo radioactive decay is predicted to be a million times more rare - and out of reach of today's technology. "This discovery highlights the extraordinary capabilities of RHIC to investigate fundamental questions about the nature of matter, antimatter, and the early universe," said William F. Brinkman, Director of the DOE Office of Science.

Steven Vigdor, Brookhaven's Associate Lab Director for Nuclear and Particle Physics, who leads the RHIC program, said, "Barring a new breakthrough in accelerator technology, or the discovery of a completely new production mechanism, it is likely that antihelium-4 will remain the heaviest stable antimatter nucleus observed for the foreseeable future."

The STAR physicists describe the discovery in a paper in Nature, published online April 24, 2011.

The ability to create and study antimatter in conditions similar to those of the early universe is no small matter: One of the great mysteries of physics is why our universe appears to be made entirely of ordinary matter when matter and antimatter are understood to have been created in equal amounts at the time of the Big Bang.

At RHIC, head-on collisions of gold ions moving at nearly the speed of light simulate conditions just after the Big Bang. In these atomic smashups, quarks and antiquarks likewise emerge with approximately equal

abundance. A major fraction of the stable antimatter produced in RHIC collisions leaves a clear signal in the STAR detector before annihilating with ordinary matter in the outer part of the experimental apparatus.

By sifting through data for half a trillion charged particles emitted from almost one billion collisions, the STAR collaboration has detected 18 examples of the unique "signature" of the antihelium-4 nucleus. Consisting of two antiprotons and two antineutrons in a stable bound state that does not undergo radioactive decay, the antihelium-4 nucleus has a negative electric charge that is twice that of an electron, while its mass is very close to four times that of a proton. Data plots show that the newly discovered anti-alphas are very cleanly separated from the lighter isotopes, and are at the expected mass.

The scientists also measured the antihelium-4 production rate in nuclear interactions, and found that it is consistent with expectations based on a statistical coalescence of antiquarks from the soup of quarks and antiquarks generated in RHIC collisions. But the fact that 12 antiquarks combine to build such a complex antinucleus in a way that bears out these predictions is really quite remarkable considering it all takes place in the midst of rapidly expanding matter created at trillions of degrees and surviving for only ten trillionths of a trillionth of a second.

Knowing the production rate of these antinuclei is important to a wide range of scientific disciplines, including searches for new phenomena in the cosmos. For example, it ties in with the scientific goals of an experiment known as the Alpha Magnetic Spectrometer (AMS), which will be delivered to the International Space Station via one of the last space shuttle missions, currently scheduled for launch in late April 2011. This experiment will search for antimatter in space.

"If AMS were to find evidence for the existence of bulk antimatter elsewhere in the cosmos, the new measurement from the STAR experiment would provide the quantitative background rate for comparison," said Hank Crawford, a STAR collaborator from the University of California, Berkeley, Space Sciences Laboratory. "An observation of antihelium-4 by the AMS experiment could indicate the existence of large quantities of antimatter somehow segregated from the matter in our universe," he said.

In 2010, the Large Hadron Collider at CERN, the European laboratory for nuclear and particle physics research, began its own collisions of heavy nuclei at energies more than an order of magnitude higher than at RHIC. Experiments there also have the capability to study production of antinuclei, and it will be interesting to see what those experiments find at higher energies.

"The discovery of the antihelium-4 nucleus also has special synergy with a major scientific anniversary: the 100th anniversary of Ernest Rutherford's seminal gold foil experiments, in which he used ordinary-matter helium-4 (alpha) particles to probe the structure of matter," said Brookhaven physicist Aihong Tang, a member of the STAR collaboration and a lead author on the Nature paper. "These experiments, conducted in 1911, established the very existence of atomic nuclei for the first time, and marked the dawn of our modern understanding of atoms."

*The STAR collaboration is composed of 54 institutions from 12 countries. Research at RHIC is funded primarily by the U.S. Department of Energy's Office of Science and by various national and international collaborating institutions, with support from many funding agencies (see: <http://www.bnl.gov/rhic/funding.asp>) Measurement capabilities vital to antihelium-4 identification were added to the STAR experiment in 2009 with the installation of a large time-of-flight detector. This device was constructed jointly by U.S. and Chinese institutions and was funded jointly by DOE's Office of Science and the National Natural Science Foundation of China, China's Ministry of Science and Technology, and the Chinese Academy of Sciences. The antihelium-4 discovery is being announced simultaneously in the U.S. and in China.*

**Related Links** \* 2010 Antimatter discovery at RHIC: [http://www.bnl.gov/bnlweb/pubaf/pr/PR\\_display.asp?prID=1075](http://www.bnl.gov/bnlweb/pubaf/pr/PR_display.asp?prID=1075)