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**New skin patch treatment kills most common form of skin cancer**  
***Radionuclide therapy study shows a novel treatment for basal cell carcinoma can cure patients without requiring hospitalization***

Miami Beach, Fla. - A customized patch treatment for basal cell carcinoma completely destroys facial tumors without surgery or major radiation therapy in 80 percent of patients studied, say researchers at the Society of Nuclear Medicine's 2012 Annual Meeting.

There are two main types of skin cancer: melanoma, which forms deep in the cells that produce pigment in skin, and nonmelanoma cancer, such as basal cell carcinoma and squamous cell carcinoma. Basal cell carcinoma is the most common type of skin cancer that affects the surface layer of the skin. Researchers have developed a treatment called a phosphorus-32 (P-32) skin patch, a radiation spot-treatment in the form of a patch that can safely and easily kill skin tumors with a few easy outpatient appointments. This therapy is ideal for patients with skin cancers that are very difficult to operate on, especially if skin grafting after surgery would be a challenge.

"The study is important for the field of nuclear medicine as it opens a new dimension in the field of therapeutic nuclear medicine and dermatology, especially for the treatment of skin malignancies," says Priyanka Gupta, Ph.D., the lead of author of the study at All India Institute of Medical Sciences, New Delhi, India. "For patients, it is beneficial because it is a simple, inexpensive and convenient procedure that does not require them to be admitted to the hospital. This may become the standard procedure for treating basal cell carcinoma or serve as an alternative when surgery and radiotherapy are not possible."

According to the World Health Organization (WHO), somewhere between two and three million nonmelanoma skin cancers develop each year around the globe, and one in every three cancers diagnosed is a skin cancer. In the United States, it is estimated that one in five Americans will develop the disease at some point in their lives. In this study, a total of 10 patients between the ages of 32 and 74 years with facial basal cell carcinoma were treated with custom-made and fully sealed P-32 patches. Subjects had lesions near the eyes, the nose and the forehead, and all were treated locally with the P-32 patch for three hours on an outpatient basis. The custom patches were reapplied on the fourth and seventh days after the first treatment for another three hours each, delivering a fragmented dose of 100 Gy (a measurement of radiation exposure) to the cancerous lesions only—without harming deeper structures or other areas of healthy skin on the face. Biopsies were taken at three months and repeated within the three years that followed treatment, and eight out of 10 patients were found to be entirely cured and cancer free.

Further research will need to be conducted before the P-32 patch can be provided for general clinical use to treat basal cell carcinoma and similar superficial skin cancers.

*Scientific Paper 62: Priyanka Gupta, Arun Malhotra and Guru Bandhopadhyaya, Nuclear Medicine, All India Institute of Medical Sciences, New Delhi, India; and Somesh Gupta, Dermatology, All India Institute of Medical Sciences, New Delhi, India, "Basal cell carcinoma treatment using Phosphorus-32 skin patches: A three year follow up study," SNM's 59th Annual Meeting, June 9, 2012, Miami Beach, Fla.*

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**Research shows humans are primary cause of global ocean warming over past 50 years**  
***The oceans have warmed in the past 50 years, but not by natural events alone.***

LIVERMORE, Calif. - New research by a team of Lawrence Livermore National Laboratory scientists and international collaborators shows that the observed ocean warming over the last 50 years is consistent with climate models only if the models include the impacts of observed increases in greenhouse gas during the 20th century.

Though the new research is not the first study to identify a human influence on observed ocean warming, it is the first to provide an in-depth examination of how observational and modeling uncertainties impact the conclusion that humans are primarily responsible.

"We have taken a closer look at factors that influence these results," said Peter Gleckler, an LLNL climate scientist and lead author of the new study that appears in the June 10 edition of the journal, *Nature Climate Change*. "The bottom line is that this study substantially strengthens the conclusion that most of the observed global ocean warming over the past 50 years is attributable to human activities."

The group looked at the average temperature (or heat content) in the upper layers of the ocean. The observed global average ocean warming (from the surface to 700 meters) is approximately 0.025 degrees Celsius per decade, or slightly more than 1/10th of a degree Celsius over 50 years. The sub-surface ocean warming is noticeably less than the observed Earth surface warming, primarily because of the relatively slow transfer of

ocean surface warming to lower depths. Nevertheless, because of the ocean's enormous heat capacity, the oceans likely account for more than 90 percent of the heat accumulated over the past 50 years as the Earth has warmed.

In this study the team, including observational experts from the United States, Japan and Australia, examined the causes of ocean warming using improved observational estimates. They also used results from a large multi-model archive of control simulations (that don't include the effects of humans, but do include natural variability), which were compared to simulations that included the effects of the observed increase in greenhouse gases over the 20th century.

"By using a "multi-model ensemble," we were better able to characterize decadal-scale natural climate variability, which is a critical aspect of the detection and attribution of a human-caused climate change signal. What we are trying to do is determine if the observed warming pattern can be explained by natural variability alone", Gleckler said. "Although we performed a series of tests to account for the impact of various uncertainties, we found no evidence that simultaneous warming of the upper layers of all seven seas can be explained by natural climate variability alone. Humans have played a dominant role."

*Livermore co-authors include Benjamin Santer, Karl Taylor and Peter Caldwell, whose work was funded by the U.S. Department of Energy (contract DE-AC52-07NA27344). International collaboration from Australia was funded through the Antarctic and Climate Ecosystems Cooperative Research Centre and the Australian Climate Change Science Program, a joint initiative of the Department of Climate Change and Energy Efficiency, the Bureau of Meteorology and CSIRO, with additional support provided from CSIRO's Wealth from Oceans Flagship. Collaborators from the U.S. are funded by Scripps Institution of Oceanography and the National Oceanic and Atmospheric Administration. Collaborators from India are funded by the Indian Institute of Technology Delhi, and collaborators from Japan are funded by the Frontier Research Center for Global Change.*

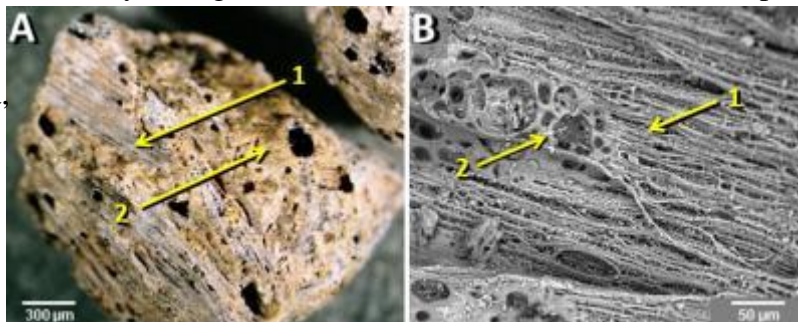
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### **Study finds new evidence supporting theory of extraterrestrial impact**

#### ***An international team has discovered melt-glass material in a thin layer of sedimentary rock in Pennsylvania, South Carolina, and Syria.***

Santa Barbara, Calif. – An 18-member international team of researchers that includes James Kennett, professor of earth science at UC Santa Barbara, has discovered melt-glass material in a thin layer of sedimentary rock in Pennsylvania, South Carolina, and Syria. According to the researchers, the material — which dates back nearly 13,000 years — was formed at temperatures of 1,700 to 2,200 degrees Celsius (3,100 to 3,600 degrees Fahrenheit), and is the result of a cosmic body impacting Earth.

These new data are the latest to strongly support the controversial Younger Dryas Boundary (YDB) hypothesis, which proposes that a cosmic impact occurred 12,900 years ago at the onset of an unusual cold climatic period called the Younger Dryas. This episode occurred at or close to the time of major extinction of the North American megafauna, including mammoths and giant ground sloths; and the disappearance of the prehistoric and widely distributed Clovis culture. The researchers' findings appear today in the Proceedings of the National Academy of Sciences.



***These are microscopic images of grains of melted quartz from the YDB cosmic impact layer at Abu Hureyra, Syria, showing evidence of burst bubbles and flow textures that resulted from the melting and boiling of rock at very high temperatures. (Light microscope image at left; SEM image at right.) Credit: UCSB***

"These scientists have identified three contemporaneous levels more than 12,000 years ago, on two continents yielding siliceous scoria-like objects (SLO's)," said H. Richard Lane, program director of National Science Foundation's Division of Earth Sciences, which funded the research. "SLO's are indicative of high-energy cosmic airbursts/impacts, bolstering the contention that these events induced the beginning of the Younger Dryas. That time was a major departure in biotic, human and climate history."

Morphological and geochemical evidence of the melt-glass confirms that the material is not cosmic, volcanic, or of human-made origin. "The very high temperature melt-glass appears identical to that produced in known cosmic impact events such as Meteor Crater in Arizona, and the Australasian tektite field," said Kennett.

"The melt material also matches melt-glass produced by the Trinity nuclear airburst of 1945 in Socorro, New Mexico," he continued. "The extreme temperatures required are equal to those of an atomic bomb blast, high enough to make sand melt and boil."

The material evidence supporting the YDB cosmic impact hypothesis spans three continents, and covers nearly one-third of the planet, from California to Western Europe, and into the Middle East. The discovery extends the range of evidence into Germany and Syria, the easternmost site yet identified in the northern hemisphere. The researchers have yet to identify a limit to the debris field of the impact.

"Because these three sites in North America and the Middle East are separated by 1,000 to 10,000 kilometers, there were most likely three or more major impact/airburst epicenters for the YDB impact event, likely caused by a swarm of cosmic objects that were fragments of either a meteorite or comet," said Kennett.

The PNAS paper also presents examples of recent independent research that supports the YDB cosmic impact hypothesis, and supports two independent groups that found melt-glass in the YDB layers in Arizona and Venezuela. "The results strongly refute the assertion of some critics that 'no one can replicate' the YDB evidence, or that the materials simply fell from space non-catastrophically," Kennett noted.

He added that the archaeological site in Syria where the melt-glass material was found — Abu Hureyra, in the Euphrates Valley — is one of the few sites of its kind that record the transition from nomadic hunter-gatherers to farmer-hunters who live in permanent villages. "Archeologists and anthropologists consider this area the 'birthplace of agriculture,' which occurred close to 12,900 years ago," Kennett said.

"The presence of a thick charcoal layer in the ancient village in Syria indicates a major fire associated with the melt-glass and impact spherules 12,900 years ago," he continued. "Evidence suggests that the effects on that settlement and its inhabitants would have been severe."

*Other scientists contributing to the research include Ted Bunch and James H. Wittke of Northern Arizona University; Robert E. Hermes of Los Alamos National Laboratory; Andrew Moore of the Rochester Institute of Technology; James C. Weaver of Harvard University; Douglas J. Kennett of Pennsylvania State University; Paul S. DeCarli of SRI International; James L. Bischoff of the U.S. Geological Survey; Gordon C. Hillman of the University College London; George A. Howard of Restoration Systems; David R. Kimbel of Kimstar Research; Gunther Kletetschka of Charles University in Prague, and of the Czech Academy of Science; Carl Lipo and Sachiko Sakai of California State University, Long Beach; Zsolt Revay of the Technical University of Munich in Germany; Allen West of GeoScience Consulting; and Richard B. Firestone of Lawrence Berkeley National Laboratory.*

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### **Sweet minty relief for cough**

#### ***Findings from the Monell Center suggest that sucrose and menthol each act independently to reduce coughing.***

PHILADELPHIA – Millions of Americans reach for their cough drops or syrup at the first sign of a cough. However, scientists are unsure if and how these popular remedies work. Now, new findings from the Monell Center suggest that sucrose and menthol, ingredients commonly regarded as flavorings in these preparations, each act independently to reduce coughing. Cough is a vital protective reflex that clears the respiratory tract of threats from mechanical stimuli like food and chemical stimuli such as airborne toxins and pollutants. As such, cough is necessary to protect the lungs, keep airways clear, and preserve life.

"Individuals with a weak cough reflex are at increased risk of pneumonia and of choking. Conversely, many acute and chronic conditions involve frequent coughing, leading to 30 million health care visits annually, with billions spent on over-the-counter medications and billions more lost due to reduced productivity," said lead author, Paul M. Wise, Ph.D., a sensory psychologist at Monell. However, many aspects of coughing remain poorly understood, including how chemicals act to trigger and modulate cough.

In the current study, which appears in the June 2012 issue of *Pulmonary Pharmacology and Therapeutics*, 12 healthy young adults inhaled from a nebulizer containing capsaicin, the burning ingredient in chili peppers and a potent chemical stimulus for cough. After each inhalation, the amount of capsaicin was doubled. This procedure continued until the subject coughed three times within 10 seconds. The capsaicin concentration that induced the three coughs was labeled as the individual's cough threshold.

In some sessions, the subjects held either a very sweet sucrose or plain water in their mouths for three seconds, spat the liquid into a sink, and then inhaled from the nebulizer.

In other sessions, subjects inhaled three breaths of either menthol-saturated air or clean air before each capsaicin inhalation. The menthol concentration was selected to approximate the cooling intensity of a menthol cigarette. Both sucrose and menthol increased the amount of capsaicin needed to elicit a cough relative to plain water or clean air, respectively. Sucrose increased cough threshold by about 45 percent, while menthol increased it by approximately 25 percent.

"This is the first study to empirically show that sweet taste reduces cough. This also is the first study to show that menthol alone can reduce coughing in response to a cough-eliciting agent," said Monell sensory scientist Paul Breslin, Ph.D., an author on the study.

The findings support the hypothesis that adding menthol to cigarettes, popularly known as "menthols," may make it easier to begin smoking by suppressing the cough reflex, thus making the first cigarettes less distressing. "Menthol may dull the sensitivity of sensory nerves in the airways and thereby actually disable an important reflex mechanism that would otherwise protect smokers from the chemical and particulate irritants present in cigarette smoke," said Wise.

Studies at Monell will continue to explore the chemical elicitation of cough, along with the receptors and genes involved in this system.

*Also contributing to the research was Pamela Dalton, Ph.D., of Monell. Breslin also holds a position as professor in the Department of Nutritional Sciences at Rutgers University. Funding was provided by the National Institute on Deafness and Other Communication Disorders of the National Institutes of Health.*

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**Kill the germs, spare the ears: How to create antibiotics that don't hurt hearing  
Apramycin, already used in animals, shows promise against drug-resistant TB and other  
'superbugs,' without hearing loss**

ANN ARBOR, Mich. - The world needs new antibiotics to overcome the ever increasing resistance of disease-causing bacteria – but it doesn't need the side effect that comes with some of the most powerful ones now available: hearing loss. Today, researchers report they have developed a new approach to designing antibiotics that kill even "superbugs" but spare the delicate sensory cells of the inner ear.

Surprisingly, they have found that apramycin, an antibiotic already used in veterinary medicine, fits this bill - setting the stage for testing in humans.

In a paper published online in the Proceedings of the National Academy of Sciences, a team from Switzerland, England and the University of Michigan show apramycin's high efficacy against bacteria, and low potential for causing hearing loss, through a broad range of tests in animals. That testing platform is now being used to evaluate other potential antibiotics that could tackle infections such as multidrug-resistant tuberculosis.

The research aims to overcome a serious limitation of aminoglycoside antibiotics, a class of drugs which includes the widely used kanamycin, gentamicin and amikacin.

While great at stopping bacterial infections, these drugs also cause permanent partial hearing loss in 20 percent of people who take them for a short course, and up to 100 percent of people who take them over months or years, for example to treat tuberculosis or lung infections in cystic fibrosis.

U-M researcher Jochen Schacht, Ph.D., a professor of biological chemistry and otolaryngology and director of the Kresge Hearing Research Institute at the U-M Medical School, has spent decades studying why these drugs cause this "ototoxicity" – a side effect that makes doctors hesitant to prescribe them. Hearing damage has also caused patients to discontinue treatment before their antibiotic prescription is over, potentially allowing drug-resistant strains of bacteria to flourish.

Schacht has found that the drugs produce damaging free radicals inside the hair cells of the inner ear. Hair cells, named for the tiny sound-sensing hairs on their surface, are the linchpin of hearing – and once destroyed, cannot be regrown.

In the new paper, Schacht and his research group joined teams led by University of Zurich microbiologist Erik Böttger, and structural biologist and Nobel Prize winner Venkatraman Ramakrishnan of England's Medical Research Council Laboratory of Molecular Biology, as well as scientists from ETH Zurich. Each team brought its particular expertise to the issue, and after four years of work they developed and tested this new approach to designing antibiotics.

"Aminoglycosides are some of the most valuable broad-spectrum antibiotics and indispensable drugs today, but we need new options to combat drug-resistant bacteria. Importantly, we must find ways to overcome their ototoxicity," Schacht says. "Instead of the trial-and-error approach of the past, this new hypothesis-driven tactic allows us to design drugs with simultaneous attention toward both antibacterial action and impact on hair cells." According to the World Health Organization, about 440,000 new cases of multidrug-resistant tuberculosis emerge annually, causing at least 150,000 deaths worldwide. Aminoglycoside antibiotics, while carefully controlled in the U.S., Europe, and other developed countries are available over the counter in many developing nations, leading to overuse that makes it even easier for drug-resistant strains of many kinds of bacteria to emerge and spread.

The new paper outlines a rational approach to designing drugs to combat this threat without ototoxicity, based on a theoretical framework that emerged from the work of the three laboratories and centers around the role of ribosomes, the structures inside the cell that "read" DNA and translate the genetic message into proteins. Böttger's lab, at the Institut für Medizinische Mikrobiologie which he directs, studies aminoglycoside effects on

mitochondrial ribosomes and antibacterial activity with an eye toward designing new ones. Ramakrishnan's lab studies ribosomes, and partners from ETH Zurich also collaborated.

Aminoglycosides bind to the ribosomes inside bacterial cells, preventing the ability to produce proteins. But while the drugs spare most human ribosomes, they can attach to ribosomes in the mitochondria of cells, which are similar to bacterial ribosomes.

Consistent with U-M-generated theories about ototoxicity, the drugs then cause the production of free radicals in such quantities that they overwhelm the hair cells' defense mechanisms – destroying the cells and causing hearing loss.

The team's approach is to design drugs that more specifically target bacterial ribosomes over mitochondrial ribosomes, simultaneously testing the impact on hair cells as well as the ability to kill bacteria. In this way, the researchers try to avoid creating antibiotics that harm hearing.

They are already using the platform employed for this study – which involves cells from mouse ears, and tests of hearing and hair cell damage in guinea pigs – to test other promising novel drugs synthesized based on the theoretical framework that was driving the current research.

Meanwhile, the team hopes to launch a clinical trial of apramycin, an antibiotic that could prove immediately useful because multidrug-resistant TB and lung-infecting bacteria have not shown resistance to the drug yet. The research also lends more evidence to support the use of antioxidants to protect the hearing of patients taking current aminoglycoside antibiotics. Schacht has already led a clinical trial in China that showed a major reduction in hearing loss if aspirin was given at the same time as aminoglycoside antibiotics. "This kind of protection is important, while we search for the long-term answer to drug resistance without ototoxicity," he says.

*Schacht's research is funded by grant DC-003685 from the National Institute on Deafness & other Communication Disorders of the National Institutes of Health. Other funding from University of Zurich, the European Community, Medical Research Council UK and the Wellcome Trust. In addition to Schacht, former U-M researchers Su-Hua Sha and Jing Xie are co-authors along with members of the two Zurich and the LMB teams. Reference [www.pnas.org/cgi/doi/10.1073/pnas.1204073109](http://www.pnas.org/cgi/doi/10.1073/pnas.1204073109)*

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**A better way to grow bone: Fresh, purified fat stem cells grow bone faster and better  
Scientists purified a subset of stem cells found in fat tissue and made from them bone that was formed faster and was of higher quality than bone grown using traditional methods**

UCLA stem cell scientists purified a subset of stem cells found in fat tissue and made from them bone that was formed faster and was of higher quality than bone grown using traditional methods, a finding that may one day eliminate the need for painful bone grafts that use material taken from the patient during invasive procedures. Adipose, or fat, tissue is thought to be an ideal source of cells called mesenchymal stem cells - capable of developing into bone, cartilage, muscle and other tissues - because they are plentiful and easily attained through procedures such as liposuction, said Dr. Chia Soo, vice chair for research at UCLA Plastic and Reconstructive Surgery. The co-senior authors on the project, Soo and Bruno Péault, are members of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA.

Traditionally, cells taken from fat had to be cultured for weeks to isolate the stem cells which could become bone, and their expansion increases risk of infection and genetic instability. A fresh, non-cultured cell composition called stromal vascular fraction (SVF) also is used to grow bone. However, SVF cells taken from adipose tissue are a highly heterogeneous population that includes cells that aren't capable of becoming bone. Péault and Soo's team used a cell sorting machine to isolate and purify human perivascular stem cells (hPSC) from adipose tissue and showed that those cells worked far better than SVF cells in creating bone. They also showed that a growth factor called NELL-1, discovered by Dr. Kang Ting of the UCLA School of Dentistry, enhanced the bone formation in their animal model.

"People have shown that culture-derived cells could grow bone, but these are a fresh cell population and we didn't have to go through the culture process, which can take weeks," Soo said. "The best bone graft is still your own bone, but that is in limited supply and sometimes not of good quality. What we show here is a faster and better way to create bone that could have clinical applications."

The study appears June 11, 2012 in the early online edition of the peer-reviewed journal Stem Cells Translational Medicine, a new journal that seeks to bridge stem cell research and clinical trials.

In the animal model, Soo and Péault's team put the hPSCs with NELL-1 in a muscle pouch, a place where bone is not normally grown. They then used X-rays to determine that the cells did indeed become bone.

"The purified human hPSCs formed significantly more bone in comparison to the SVF by all parameters," Soo said. "And these cells are plentiful enough that patients with not much excess body fat can donate their own fat tissue."

Soo said if everything goes well, patients may one day have rapid access to high quality bone graft material by which doctors get their fat tissue, purify that into hPSCs and replace their own stem cells with NELL-1 back into the area where bone is required. The hPSC with NELL-1 could grow into bone inside the patient, eliminating the need for painful bone graft harvestings. The goal is for the process to isolate the hPSCs and add the NELL-1 with a matrix or scaffold to aid cell adhesion to take less than an hour, Soo said.

"Excitingly, recent studies have already demonstrated the utility of perivascular stem cells for regeneration of disparate tissue types, including skeletal muscle, lung and even myocardium," said Péault, a professor of orthopedic surgery "Further studies will extend our findings and apply the robust osteogenic potential of hPSCs to the healing of bone defects."

*The study was funded in part by the California Institute of Regenerative Medicine Early Translational Research Award and Training Grant Research Fellowship, a University of California Discovery Grant and the National Institute of Dental and Craniofacial Research Center at the National Institutes of Health (R21-DE0177711 and RO1-DE01607).*

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### **Moderation as the Sweet Spot for Exercise**

***Moderate exercise may be more beneficial than vigorous workouts.***

**By GRETCHEN REYNOLDS**

For people who exercise but fret that they really should be working out more, new studies may be soothing. The amount of exercise needed to improve health and longevity, this new science shows, is modest, and more is not necessarily better.

That is the message of the newest and perhaps most compelling of the studies, which was presented on Saturday at the annual meeting of the American College of Sports Medicine in San Francisco. For it, researchers at the University of South Carolina Arnold School of Public Health and other institutions combed through the health records of 52,656 American adults who'd undergone physicals between 1971 and 2002 as part of the Aerobics Center Longitudinal Study at the Cooper Institute in Dallas. Each participant completed physical testing and activity questionnaires and returned for at least one follow-up visit.

The researchers found that about 27 percent of the participants reported regularly running, although in wildly varying amounts and paces.

The scientists then checked death reports.

Over the course of the study, 2,984 of the participants died. But the incidence was much lower among the group that ran. Those participants had, on average, a 19 percent lower risk of dying from any cause than non-runners. Notably, in closely parsing the participants' self-reported activities, the researchers found that running in moderation provided the most benefits. Those who ran 1 to 20 miles per week at an average pace of about 10 or 11 minutes per mile - in other words, jogging - reduced their risk of dying during the study more effectively than those who didn't run, those (admittedly few) who ran more than 20 miles a week, and those who typically ran at a pace swifter than seven miles an hour.

"These data certainly support the idea that more running is not needed to produce extra health and mortality benefits," said Dr. Carl J. Lavie, medical director of cardiac rehabilitation and prevention at the Ochsner Medical Center in New Orleans and an author of the study. "If anything," he continued, "it appears that less running is associated with the best protection from mortality risk. More is not better, and actually, more could be worse."

His analysis echoes the results of another new examination of activity and mortality, in which Danish scientists used 27 years' worth of data collected for the continuing Copenhagen City Heart Study. They reported that those Danes who spent one to two and a half hours per week jogging at a "slow or average pace" during the study period had longer life spans than their more sedentary peers and than those who ran at a faster pace. This decidedly modest amount of exercise led to an increase of, on average, 6.2 years in the life span of male joggers and 5.6 years in women.

"We can say with certainty that regular jogging increases longevity," Dr. Peter Schnorr, a cardiologist and an author of the study, said in presenting the findings at a clinical meeting organized last month by the European Association for Cardiovascular Prevention and Rehabilitation. "The good news is that you don't actually need to do that much to reap the benefits."

"The relationship appears much like alcohol intakes," he continued. "Mortality is lower in people reporting moderate jogging than in non-joggers or those undertaking extreme levels of exercise."

There's further confirmation of that idea in the findings of a large study of exercise habits published last year in *The Lancet*, which showed that among a group of 416,175 Taiwanese adults, 92 minutes a week of moderate exercise, like walking, gentle jogging or cycling, increased life span by about three years and decreased the risk of mortality from any cause by about 14 percent.

In that study, those who embarked on more ambitious exercise programs did gain additional risk reduction, as seems only fair, but the benefits plateaued rapidly. For each further 15 minutes per week of moderate exercise that someone completed beyond the first 92, his or her mortality risk fell, but by only about another 4 percent. Whether and at what point more exercise becomes counterproductive remains uncertain. "In general, it appears that exercise, like any therapy, results in a bell-shaped curve in terms of response and benefit," says Dr. James H. O'Keefe, a cardiologist and lead author of a thought-provoking review article published on Monday in *Mayo Clinic Proceedings* that examines whether extreme amounts of vigorous exercise, particularly running, can harm the heart.

"To date, the data suggests that walking and light jogging are almost uniformly beneficial for health and do increase life span," Dr. O'Keefe says. "But with more vigorous or prolonged exercise, the benefits can become questionable. "I'm a fan of distance running," he adds. "I run. But after about 45 to 60 minutes a day, you reach a point of diminishing returns, and at some point, you risk toxicity."

His advice? The study by Dr. Lavie and his colleagues offers excellent guidelines for safe and effective exercise, Dr. O'Keefe says. "Twenty miles a week or less of jogging at a 10- or 11-minute-mile pace can add years to your life span. That's very good news." Indeed it is - especially since that routine happens to replicate almost exactly my own weekly exercise regimen. "I wouldn't automatically discourage people from doing more if they really want to" and are not experiencing side effects, like extreme fatigue or repeated injuries, Dr. O'Keefe continued. "But the message from the latest data is that the sweet spot for exercise seems to come with less." *Gretchen Reynolds is the author of "The First 20 Minutes: Surprising Science Reveals How We Can Exercise Better, Train Smarter, Live Longer" (Hudson Street Press, 2012).*

*This post has been revised to reflect the following correction: Correction: June 11, 2012*

*An earlier version of this column misidentified the study population in a report published last year in The Lancet that found that moderate exercise increased life span. The study subjects were Taiwanese, not Korean.*

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### **New study shows earlier birth is best for twins**

***University of Adelaide researchers say women pregnant with twins should elect to give birth at 37 weeks to avoid serious complications.***

The advice is based on the world's biggest study addressing the timing of birth for women who have an uncomplicated twin pregnancy, the results of which are published today in the *British Journal of Obstetrics & Gynaecology*.

Studying 235 women in Australia, New Zealand and Italy, researchers found that babies born to women in the early birth group (37 weeks) were significantly less likely to be small for their gestational age compared with babies born to women in the standard care group (38 weeks or later).

Lead researcher Professor Jodie Dodd from the University of Adelaide's Robinson Institute and the Women's & Children's Hospital says: "Infants of a twin pregnancy are recognized to be at risk of problems during pregnancy, particularly from a slowing of the rate of growth in one or both twins.

"This slowing of the growth rate can result in low birth weight, which is associated with an increased need for care in the neonatal nursery in the short term and increased risk of health problems in later life, including heart disease and diabetes. There is also the risk of one or both twins being stillborn.

"This is why we've taken such a great interest in the optimal time for twins' birth," Professor Dodd says.

"We found that at 37 weeks, elective birth is associated with a significant reduction in the risk of serious morbidity for infants, without increasing complications related to immaturity or induction of labor."

Professor Dodd says there has been a lot of uncertainty in clinical practice about the optimal time for twins' birth.

"We hope this study will help clinicians to make recommendations to women with healthy twin pregnancies that lead to less complications at birth, and therefore lead to happier, healthier lives for their babies.

"While this is the biggest study of its kind so far, our research supports the evidence shown in previous studies, and it also supports the guidelines of care released by the Royal College of Obstetricians & Gynaecologists in September 2011. These guidelines recommend that women who have uncomplicated twin pregnancies should elect to give birth at 37 weeks."

*This study was supported by a grant from the Women's and Children's Hospital Foundation.*

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**Role of omega-3 in preventing cognitive decline in older people questioned**  
***Older people who take omega-3 fish oil supplements are probably not reducing their chances of losing cognitive function***

Older people who take omega-3 fish oil supplements are probably not reducing their chances of losing cognitive function, according to a new Cochrane systematic review. Based on the available data from studies lasting up to 3.5 years, the researchers concluded that the supplements offered no benefits for cognitive health over placebo capsules or margarines, but that longer term effects are worth investigating.

Omega-3 fatty acids are fats responsible for many important jobs in the body. We get these fats through our daily diets and the three major omega-3 fats are: alpha linolenic acid (ALA) from sources such as nuts and seeds and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) from sources including oily fish such as salmon and mackerel. A number of studies have hinted that omega-3 fatty acids and DHA in particular may be involved in keeping nerve cells in the brain healthy into old age. However, there is limited evidence for the role of these fats in preventing cognitive decline and dementia.

The researchers, led by Emma Sydenham at the London School of Hygiene & Tropical Medicine (LSHTM), London, UK, gathered together evidence from three high quality trials comparing the effects of omega-3 fatty acids taken in capsules or margarine spread to those of sunflower oil, olive oil or regular margarine. A total of 3,536 people over the age of 60 took part in the trials, which lasted between six and 40 months. None of the participants had any signs of poor cognitive health or dementia at the start of the trials.

The researchers found no benefit of taking the omega-3 capsules or spread over placebo capsules or spread. Participants given omega-3 did not score better in standard mental state examinations or in memory and verbal fluency tests than those given placebo.

"From these studies, there doesn't appear to be any benefit for cognitive health for older people of taking omega-3 supplements," said Alan Dangour, a nutritionist at LSHTM and co-author of the report. "However, these were relatively short-term studies, so we saw very little deterioration in cognitive function in either the intervention groups or the control groups. It may take much longer to see any effect of these supplements." The researchers conclude that the longer term effects of omega-3 fatty acids on cognitive decline and dementia need to be explored in further studies, particularly in people with low intakes of omega-3 fatty acids in their diet. In the meantime, they stress other potential health benefits. "Fish is an important part of a healthy diet and we would still support the recommendation to eat two portions a week, including one portion of oily fish," said Dangour.

[http://www.eurekalert.org/pub\\_releases/2012-06/sfpa-afl061112.php](http://www.eurekalert.org/pub_releases/2012-06/sfpa-afl061112.php)

**A father's love is one of the greatest influences on personality development**  
***A father's love contributes as much - and sometimes more - to a child's development as does a mother's love.***

That is one of many findings in a new large-scale analysis of research about the power of parental rejection and acceptance in shaping our personalities as children and into adulthood.

"In our half-century of international research, we've not found any other class of experience that has as strong and consistent effect on personality and personality development as does the experience of rejection, especially by parents in childhood," says Ronald Rohner of the University of Connecticut, co-authored the new study in *Personality and Social Psychology Review*. "Children and adults everywhere - regardless of differences in race, culture, and gender - tend to respond in exactly the same way when they perceived themselves to be rejected by their caregivers and other attachment figures."

Looking at 36 studies from around the world that together involved more than 10,000 participants, Rohner and co-author Abdul Khaleque found that in response to rejection by their parents, children tend to feel more anxious and insecure, as well as more hostile and aggressive toward others. The pain of rejection - especially when it occurs over a period of time in childhood - tends to linger into adulthood, making it more difficult for adults who were rejected as children to form secure and trusting relationships with their intimate partners. The studies are based on surveys of children and adults about their parents' degree of acceptance or rejection during their childhood, coupled with questions about their personality dispositions.

Moreover, Rohner says, emerging evidence from the past decade of research in psychology and neuroscience is revealing that the same parts of the brain are activated when people feel rejected as are activated when they experience physical pain. "Unlike physical pain, however, people can psychologically re-live the emotional pain of rejection over and over for years," Rohner says.



When it comes to the impact of a father's love versus that of a mother, results from more than 500 studies suggest that while children and adults often experience more or less the same level of acceptance or rejection from each parent, the influence of one parent's rejection - oftentimes the father's - can be much greater than the other's. A 13-nation team of psychologists working on the International Father Acceptance Rejection Project has developed at least one explanation for this difference: that children and young adults are likely to pay more attention to whichever parent they perceive to have higher interpersonal power or prestige. So if a child perceives her father as having higher prestige, he may be more influential in her life than the child's mother. Work is ongoing to better understand this potential relationship.

One important take-home message from all this research, Rohner says, is that fatherly love is critical to a person's development. The importance of a father's love should help motivate many men to become more involved in nurturing child care. Additionally, he says, widespread recognition of the influence of fathers on their children's personality development should help reduce the incidence of "mother blaming" common in schools and clinical setting. "The great emphasis on mothers and mothering in America has led to an inappropriate tendency to blame mothers for children's behavior problems and maladjustment when, in fact, fathers are often more implicated than mothers in the development of problems such as these."

*The paper "Transnational Relations Between Perceived Parental Acceptance and Personality Dispositions of Children and Adults: A Meta-Analytic Review" was published in the May 2012 Personality and Social Psychology Review, a journal of the Society for Personality and Social Psychology (SPSP).*

<http://phys.org/news/2012-06-basic-blocks-life-rethought.html>

**The basic building blocks of life to be rethought after one discovered to be missing  
A gene thought previously to be present in all life on earth has been found to be missing in life  
near volcanoes.**

Phys.org - The protein, thought to be one of the fundamental building-blocks of life, is not present in certain volcanic single cell organisms. The scientists studied archaea, which are similar to bacteria, but have an independent evolutionary history, for the research. The research published in the Proceedings of the National Academy of Sciences (PNAS) found the expected gene missing and another in its place.

This missing protein, named SSB, performs an essential role binding DNA and protecting it from damage. Professor Malcolm White of the School of Biology at the University of St Andrews said: "All cells, whether they are microbial or human, have some things in common. "These are the fundamental components or building blocks which were present in the first cells and have been passed on over 3.5 billion years. "However, we have discovered that a gene normally thought to be absolutely essential and conserved throughout every form of life, is in fact lost in one group of volcanic bugs, and replaced by a completely novel gene we have christened ThermoDBP." The discovery has ramifications for understanding about how life has evolved on earth.

The new gene could have applications in biotechnology and the new scientific discipline of synthetic biology. More information: Displacement of the canonical single-stranded DNA-binding protein in the Thermoproteales, PNAS, Published online before print November 21, 2011, doi: 10.1073/pnas.1113277108

**Abstract**

*ssDNA-binding proteins (SSBs) based on the oligonucleotide-binding fold are considered ubiquitous in nature and play a central role in many DNA transactions including replication, recombination, and repair. We demonstrate that the Thermoproteales, a clade of hyperthermophilic Crenarchaea, lack a canonical SSB. Instead, they encode a distinct ssDNA-binding protein that we term "ThermoDBP," exemplified by the protein Ttx1576 from Thermoproteus tenax. ThermoDBP binds specifically to ssDNA with low sequence specificity. The crystal structure of Ttx1576 reveals a unique fold and a mechanism for ssDNA binding, consisting of an extended cleft lined with hydrophobic phenylalanine residues and flanked by basic amino acids. Two ssDNA-binding domains are linked by a coiled-coil leucine zipper. ThermoDBP appears to have displaced the canonical SSB during the diversification of the Thermoproteales, a highly unusual example of the loss of a "ubiquitous" protein during evolution. Provided by University of St Andrews*

<http://arstechnica.com/science/2012/06/new-open-access-journal-aims-to-disrupt-scholarly-publishing/>

**Pay (less) to publish: ambitious journal aims to disrupt scholarly publishing**

**PeerJ promises peer review and open access for just \$99.**

**by John Timmer - June 12 2012, 10:00pm TST**

The push to open access to scientific publications has seen some remarkable successes this year. After publishers appeared to overreach by pushing to revoke the US government's existing open access policy, researchers started boycotting one of the bill's backers. A competing bill was introduced that would compel more government agencies to make their work available via open access, and a similar White House petition has received over 25,000 signatures. Even the editor-in-chief of Nature now considers open access an inevitability.

Publishers that offer open access options need to recoup their costs without subscription fees, however, and had researchers pay for their publications with charges that are generally over \$1,000. Now, a new open access journal is being launched that aims to turn the finances on their head. Researchers will only have to pay a one-time fee of \$259 to gain lifetime publishing privileges in the journal, which will focus on biology research. Ars talked to the publisher, Peter Binfeld, to find out how the new peer-reviewed, biology-focused PeerJ will work. Binfeld believes that open access to research has reached an inflection point. "It feels like we've turned a hockey-stick corner of a disruption curve, and open access is now picking up, and I think everyone can see that," he said. Unfortunately, open access publishing, though free for readers, costs researchers a lot of money. PeerJ is a "great opportunity to experiment with a different business model, a different payment model." Binfeld was formerly at the open access publisher Public Library of Science managing its PLoS One journal, which charges its authors \$1,350 to publish—and it's one of the cheaper PLoS journals (fees go up to \$2,900 at other PLoS journals). PNAS, a traditional journal, charges roughly the same amount to provide open access to one of its papers, and that's on top of the usual per-page and per-figure fees charged for the print version. All of which makes PeerJ's pricing model nothing short of jaw-dropping. For a one-time \$99 fee, anyone can publish a single paper a year for life (although the first dozen authors on the paper all have to sign up). \$259 buys any author a lifetime membership, with the ability to publish as many papers as they choose. Bottom line: for only a fraction of the cost of a regular publication, researchers can publish as often as they want. "It flips the model from payment-for-publication to a membership model," Binfeld said, "where someone gets a membership for life and gets free publications thereafter."

### **A new approach**

How can this possibly work? Binfeld's answer suggests that he has run the numbers carefully. Part of the solution relies on the dynamics of authorship: not everyone will publish all of their papers in PeerJ, and some people will publish a couple of papers and then leave research. Most papers in biology have multiple authors, too, which will help drive membership.

PeerJ has also figured out how to cut costs. The journal will use customized software to manage the article submission and peer review process, and journal content will be stored on Amazon's S3 service and presented to users via software running on EC2. For long-term archiving, the publication will be placed at the National Institutes of Health's PubMed Central archive. According to Binfeld's partner, Jason Hoyt, they've got a couple of servers for internal use, but everything user-facing will run on Amazon's hardware. "When you do all the math, the revenue works out," Binfeld said, "and the costs need to be kept as low as possible."

Other aspects that add to the costs of traditional journals, like news and commentary, will not make an appearance in PeerJ. The journal will follow PLoS one's model: research will be judged on the scientific validity of the experiments, and the journal won't focus on the probable impact or significance of the work. The plan is to ensure that review is completed within a month of the article's submission.

PeerJ's involvement can, at the authors' choice, also start well before a paper is submitted for review. The journal will run a preprint server where researchers can place drafts and works-in-progress—common practice in the physics community, but not yet popular among biologists. Binfeld says PeerJ hopes to make the practice more appealing by giving users fine-grained control over sharing, letting them limit who has access to papers prior to publication. Authors also get the chance to share the title and/or abstract, which Binfeld suggested can help authors claim precedence for being the first to report some results.

Although the pricing and open access are appealing, PeerJ's plan is really to build up a sense of community within the researchers who publish there. "By doing this," Binfeld said, "we will have a community of members, of peers, rather than a collection of one-off customers who publish a paper with us, and we charge them money, they leave, and we don't care about them, we don't see them again." PeerJ will try to leverage this sense of community - Binfeld referred to having "members in good standing" who were involved in peer review for the journal.

PeerJ also plans to do peer review a bit differently. Members won't get credit for any peer review they do anonymously, which is part of a plan to encourage an open peer review system. "We're trying to encourage open peer review, and that really has two aspects," Binfeld said. "You can openly provide your identity as a reviewer. The other end of open peer review is to provide the entire peer review history on the published paper, and we're going to encourage but not require both of them." (That history includes the reviewers' comments and any changes made in response to them.)

PeerJ is trying many new things at once, and it's not clear all of them will succeed. Still, the most radical change—the low price—is sure to attract some people who are willing to give it a try. The journal also has an excellent pedigree, with Binfeld's experience at PLoS paired with that of cofounder Jason Hoyt, who worked at

community reference management site Mendeley. The team has also picked up the backing of open access aficionado Tim O'Reilly. So even if all their different endeavors don't pan out, the effort still has the potential to be disruptive.

<http://www.sciencedaily.com/releases/2012/06/120612101613.htm>

**Groundbreaking Discovery of the Cellular Origin of Cervical Cancer**  
***Scientists, with clinicians have identified a unique set of cells in the cervix that are the cause of human papillomaviruses related cervical cancers.***

ScienceDaily - A team of scientists from A\*STAR's Institute of Medical Biology (IMB) and Genome Institute of Singapore (GIS) together with clinicians from Boston's Brigham and Women's Hospital (BWH) have identified a unique set of cells in the cervix that are the cause of human papillomaviruses (HPV) related cervical cancers. Significantly, the team also showed that these cells do not regenerate when excised. These findings have immense clinical implications in the diagnosis, prevention and treatment of cervical cancer.

The study was published in the Proceedings of the National Academy of Sciences (PNAS), this week.

Cervical cancer is the 7th most common female cancer in Singapore and about 200 cases are diagnosed every year.[1] Infection with HPV is the most common cause or risk factor for cervical cancer. HPV infection causes pre-invasive cancer, termed CIN (Cervical Intraepithelial Neoplasia), which are pre-cancerous lesions that can progress and potentially become invasive cancer if left untreated.

Dr Christopher P. Crum, Director of Women's and Perinatal Pathology in the Department of pathology at BWH, said, "It has been a decades-old mystery why cervical cancers caused by HPV arise only from a discrete region of the cervix, known as the 'squamocolumnar junction', despite the presence of the virus throughout the genital tract.

The discovery of these cells finally resolves this mystery and will have wide-ranging impact from developing more meaningful animal models of early cervical carcinogenesis to clinical implications."

The team discovered that this discrete set of cells, located at the squamocolumnar junction of the cervix, uniquely express biomarkers that are seen in all forms of invasive cervical cancers linked to HPV. This means that the signature markers of this population of cells can provide a way of distinguishing potentially dangerous precancerous lesions from those with a benign prognosis.

Dr Wa Xian, Principal Investigator at IMB, said, "Our study also revealed that this exotic population of cells does not reappear after ablation[2] by cone biopsy.

This finding helps to explain the low rate of new HPV infections in the cervix after excisional therapy and also raises the distinct possibility that preemptive removal of these cells in young women could reduce their risk of cervical cancer. This could be an alternative to current vaccines which only protect against HPV 16 and 18."

This study further validates previous work[3] by Dr Xian and Dr McKeon in collaboration with BWH and NUS, which showed for the first time that some cancers originate from just a small set of cells that are unique from the other cells that reside around them.

Dr Frank Mckeon, Senior Group Leader at GIS, said, "Our previous work on esophageal cancer opened up the possibility of 'preventive therapy' to stamp out the disease by eliminating this small group of cells.

This recent work in the cervix further validates this concept and raises important possibilities for early intervention to prevent malignancies linked to very small populations of these unusual, discrete population of cells."

Prof Birgitte Lane, Executive Director of IMB, said, "This compelling study lends further weight to the importance of specific target cell populations underlying cancer. It is a powerful example of what can be done by combining skilled pathology with modern molecular genetics to uncover important new information, even in such a well-studied disease as cervical cancer."

Notes:

[1]<http://www.singhealth.com.sg/PatientCare/ConditionsAndTreatments/Pages/Cervical-Cancer-Cervix-Cancer.aspx>

[2] Cervical ablation is the removal of some of the outer layers of the cervix. Gynecologists perform cervical ablation when there is evidence or suspicion of cervical cancer.

[3] This paper can be found in the 24 June, 2011 advance online issue of Cell entitled "Residual Embryonic Cells as Precursors of a Barrett's-Like Metaplasia."

The above story is reprinted from materials provided by Agency for Science, Technology and Research (A\*STAR), Singapore. M. Herfs, Y. Yamamoto, A. Laury, X. Wang, M. R. Nucci, M. E. McLaughlin-Drubin, K. Munger, S. Feldman, F. D. McKeon, W. Xian, C. P. Crum. A discrete population of squamocolumnar junction cells implicated in the pathogenesis of cervical cancer. Proceedings of the National Academy of Sciences, 2012; DOI: 10.1073/pnas.1202684109

**Evidence That Man Cured of HIV Harbors Viral Remnants Triggers Confusion**  
***Cured? Researchers are disagreeing about how to interpret sensitive tests suggesting that HIV might still be present in man believed cured.***

by Jon Cohen on 11 June 2012, 5:51 PM | 6 Comments

Only one person ever has been cured of an HIV infection, and a presentation about the man at a scientific meeting in Sitges, Spain, last week has caused an uproar about the possibility that he's still infected. Timothy Brown, initially referred to as "the Berlin patient" until he went public about his cure, received unusual blood transplants 5 years ago to treat his leukemia. The blood came from a donor who had mutant cells resistant to HIV. Following the procedure, Brown stopped taking antiretrovirals (ARVs), the virus never returned, and his doctors reported that he had been cured.

But new research presented on 8 June at the International Workshop on HIV & Hepatitis Virus "challenge[s] these results," asserts Alain Lafeuillade of the General Hospital in Toulon, France, a well known HIV/AIDS cure researcher.

Lafeuillade issued a press release, "The So Called HIV Cured 'Berlin' Patient Still Has Detectable HIV in His Body," that questions whether Brown was reinfected and may still be infectious to other people. Lafeuillade also posted a blog item, "The Weird Story of the Berlin Patient," raising similar questions.

The scientists who conducted the new study strongly object to Lafeuillade's interpretation of their results. "We weren't trying to say HIV was still there or he hadn't been cured," says virologist Steven Yukl of the University of California, San Francisco, who gave the talk.

Yukl, who works in Joseph Wong's lab, highlighted the difficulties that they and several labs they collaborated with have had determining if Brown truly had eradicated the virus from his body. "There are some signals of the virus and we don't know if they are real or contamination, and, at this point, we can't say for sure whether there's been complete eradication of HIV," says Yukl. "The point of the presentation was to raise the question of how do we define a cure and, at this level of detection, how do we know the signal is real?"

Using sensitive polymerase chain reaction (PCR) tests to scour through Brown's blood cells, plasma, and rectal tissue, Yukl and others were able to detect bits of viral nucleic acid. Although Yukl and others who plucked out positive signals believe they are real signs of HIV, Douglas Richman of the University of California, San Diego, another collaborator, found nothing and suspects his colleagues have found contaminants. "If you do enough cycles of PCR, you can get a signal in water for pink elephants," says Richman. Another lab also found HIV antibodies in Brown, though levels were low and declining.

Tae-Wook Chun, of the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland, is one of the collaborators who found positive signals for HIV, but he stresses that no one isolated virus that could copy itself, and suggests Brown may simply harbor harmless, defective genetic pieces of the virus. "We're pushing the limits of detection," says Chun. "At the end of the day it's clear to us that he has some pretty low residual viremia. I don't really know what to make out of it, other than he's controlling viral replication or he doesn't have HIV that can restart the infection. It's a difficult case to talk about."

Ideally, the researchers would have shown that the viral pieces they found matched the virus that was previously in Brown.

But no such evidence exists. Chun and another collaborator, Robert Siliciano of the Johns Hopkins University School of Medicine in Baltimore, Maryland, did sequence bits of virus they recovered, but the genetic codes did not match each other—or the virus found in Brown before his transplant. Yukl notes that the cloning was done from blood cells and involves repeated PCRs. "There's a huge potential for contamination," Yukl says, stressing that the sequences from blood cells do not necessarily invalidate the signals from plasma and gut.

To Lafeuillade, the mismatched sequences suggested that Brown may have cleared the virus and then become reinfected. He also wondered why Brown still had any antibodies to the virus at all. "I am just asking scientific questions that nobody seems to be able/or to want to ask," says Lafeuillade in an e-mail.

Richman, who chaired the session at the meeting that included Yukl's talk, says Lafeuillade "completely misinterpreted" a thoughtful presentation and subsequent discussion—and that it in no way challenges whether Brown is cured. "[Brown's] been off ARVs for 5 years," says Richman. "That trumps all these assays."

*This item was updated on 12 June at 1:45 p.m. to clarify the techniques used to look for viral material, and Steven Yukl's perspective on the results.*

## **Diesel Exhaust Fumes Can Cause Cancer**

***Diesel engine exhaust fumes can cause cancer in humans and belong in the same potentially deadly category as asbestos, arsenic and mustard gas, experts said on Tuesday.***

**By Kate Kelland**

LONDON (Reuters) - Diesel engine exhaust fumes can cause cancer in humans and belong in the same potentially deadly category as asbestos, arsenic and mustard gas, World Health Organisation (WHO) experts said on Tuesday. In an announcement that caused consternation among car and truck makers, the France-based International Agency for Research on Cancer (IARC), part of the WHO, reclassified diesel exhausts from its group 2A of probable carcinogens to its group 1 of substances that have definite links to cancer.

The experts, who said their decision was unanimous and based on "compelling" scientific evidence, urged people across the world to reduce their exposure to diesel fumes as much as possible. "The (expert) working group found that diesel exhaust is a cause of lung cancer and also noted a positive association with an increased risk of bladder cancer," it said in a statement.

The decision is a result of a week-long meeting of independent experts who assessed the latest scientific evidence on the cancer-causing potential of diesel and gasoline exhausts. The decision puts diesel fumes in the same risk category as a number of other noxious substances including asbestos, arsenic, mustard gas, alcohol and tobacco.

Christopher Portier, chairman of the IARC working group, said the group's conclusion "was unanimous, that diesel engine exhaust causes lung cancer in humans". "Given the additional health impacts from diesel particulates, exposure to this mixture of chemicals should be reduced worldwide," he said in a statement.

### **Public Health Issue**

Diesel cars are mainly popular in western Europe, where tax advantages have encouraged technological advances and a boom in demand. Outside of Europe and India, diesel engines are almost entirely confined to commercial vehicles - mostly because of the fuel's greater efficiency. German carmakers are trying to raise awareness for diesels in the United States, where the long distances travelled on highways suit diesel engines. IARC noted that large populations all over the world are exposed to diesel exhaust in everyday life, whether through their jobs or in ambient air. "People are exposed not only to motor vehicle exhausts but also to exhausts from other diesel engines...(such as diesel trains and ships) and from power generators," it said.

IARC's director Christopher Wild said that against this background, Tuesday's conclusion "sends a strong signal that public health action is warranted". "This emphasis is needed globally, including among the more vulnerable populations in developing countries where new technology and protective measures may otherwise take many years to be adopted," he said in a statement.

### **Diesel Has Cleaned Up**

For about 20 years, diesel engine exhaust was defined by IARC as probably carcinogenic to humans - group 2A - but an IARC advisory group has repeatedly recommended diesel engine exhaust as a high priority for re-evaluation since 1998. The global auto industry had argued diesel fumes should be given a less high-risk rating to reflect tighter emissions standards.

Reacting to the decision, Allen Schaeffer, executive director of the Washington-based Diesel Technology Forum said diesel engine and equipment makers, fuel refiners and emissions control technology makers have invested billions of dollars in research into technologies and strategies to reduce emissions.

"New technology diesel engines, which use ultra-low sulphur diesel fuel, advanced engines and emissions control systems, are near zero emissions for nitrogen oxides, hydrocarbons and particulate matter," he said in a statement.

A spokeswoman for the European Automobile Manufacturers' Association said she was surprised by the move and the industry would "have to study the findings in all their details". "These technologies have been developed to address precisely these concerns," Sigrid de Vries told Reuters. "The latest diesel technology is really very clean."

IARC said it had considered recent advances in technology which had cut levels of particulates and chemicals in exhaust fumes, particularly in developed economies, but said it was not yet clear how these might translate into health effects. "Research into this question is needed," it said. "In addition, existing fuels and vehicles without these modifications will take many years to be replaced, particularly in less developed countries, where regulatory measures are currently also less stringent."

IARC said gasoline exhaust fumes should be classified as "probably carcinogenic to humans", a finding that was unchanged from its previous assessment in 1989.

[http://www.eurekalert.org/pub\\_releases/2012-06/acs-1ad061312.php](http://www.eurekalert.org/pub_releases/2012-06/acs-1ad061312.php)

**1960s-era anti-cancer drug points to treatments for Lou Gehrig's disease**  
***A long-used anti-cancer drug could be a starting point to develop treatments for amyotrophic lateral sclerosis***

A long-used anti-cancer drug could be a starting point to develop new treatments for the incurable nerve disease known as Lou Gehrig's disease or amyotrophic lateral sclerosis (ALS), scientists are reporting. Their research showing how the drug prevents clumping of an enzyme linked to ALS appears in the Journal of the American Chemical Society.

Lucia Banci, Ivano Bertini and colleagues explain that ALS causes a progressive loss of muscle control as the nerves that control body movements wither and die. Patients become weak and have difficulty swallowing and breathing, and most die within three to five years of diagnosis. Although some ALS cases are hereditary and run in families, about 90 percent are "sporadic," with the cause unknown. Some research links sporadic ALS to clumping of an antioxidant enzyme called hSOD1. The authors explored whether cisplatin, a chemotherapy drug used since the 1960s that is known to interact with some of the enzyme's amino acids, has any effect on hSOD1 clusters.

The scientists found that in laboratory tests, the anti-cancer drug cisplatin bound readily to the enzyme, preventing hSOD1 from aggregating and dissolving existing bunches. Cisplatin targets sites that can form bonds between hSOD1 after the enzyme loses the atom of copper it normally carries. The scientists note that cisplatin does not prevent the enzyme from performing its normal functions. "From this work it appears that cisplatin is a promising lead compound for the rational design of ALS treatments," the authors say.

*The authors acknowledge funding from the Italian Research Project of National Interest (PRIN) and Bio-NMR.*

<http://phys.org/news/2012-06-critical-role-granite-evolution-life.html>

**Critical role of granite in evolution of life on Earth revealed in new study**  
***It's one of the world's toughest forms of rock, used to create buildings and monuments across the globe, and famously linked with one of Scotland's main cities.***

Now scientists have discovered that granite played an important role in a major episode over 1.5 billion years ago, which eventually led to human life on Earth. Findings from a study led by the University of Aberdeen in collaboration with the Scottish Universities Environmental Research Centre published in *Geology*, reveal that the shift from simple to more complex life on this planet was prompted by the high prevalence of granite in the Earth's crust at this time.

Professor John Parnell from the University of Aberdeen's School of Geosciences said: "Over 1.5 billion years ago a major transition took place which resulted in the evolution of life from single-celled organisms – the simplest, most basic form of life— into much more complex, multi-celled organisms.

"Our findings have made the link for the first time that it was the vast amount of granite in the Earth's crust at this point, which helped this shift to occur. "The Earth's crust 1.5 billion years ago was particularly thick which in turn meant that it was extremely hot, as the deeper you extend into the Earth, the hotter the temperature. "The rocks within the crust which melted due to this heat rose to the surface where they cooled and formed granite.

"Metals prevalent in this granite – especially zinc, copper and molybdenum – were eroded at the surface of the Earth and incorporated into the simple cells which were the predominant form of life on the planet at this point."

"It was the introduction of the metals into these single-celled organisms that changed their chemistry and allowed them to evolve into the complex multi-celled organisms which were the first step towards more diverse life on Earth. "When a cell is more complex it means it can perform more functions – and one of the new functions of the complex multi-celled organisms which developed at this time, was sexual reproduction.

"The mixing of genes which are a result of sexual reproduction, give the variations that allow for natural selection, which drives evolution. "What our findings have revealed is that without the high density of granite, there would not have been enough metal to allow these cells to become more complex, and ultimately this key point in evolution which eventually led to human life on Earth, could not have taken place at that time."

The scientists derived evidence for their findings from metal ore deposits found in 1.5 to 1.8 billion year-old rocks in many parts of the world, but in particular Australia. Small scale versions of similar rock types with traces of metal are also evident on the mainland of the North West of Scotland and the Hebrides.

Dr. Adrian Boyce from the Scottish Universities Environmental Research Centre said: "It's a privilege to be able to work on rocks such as these, which are opening up the secrets of key transitions in the life of our planet."

## **Human Microbiome Project finds vast individuality in healthy human bacterial populations**

### ***A multi-year effort the Human Microbiome Project has announced first genomic compilation of the generalized biome of microbes in the human body that complement the human genome.***

When researchers at NIH and Celera published the first complete draft sequences of the human genome in 2001, many people assumed that the genetic foundation for a new and complete understanding of the human body and its functions had been achieved. As it turned out this was far from the complete story, since it turns out that our bodies are, well... not completely human.

In the culmination of a multi-year effort directed by NIH, the Human Microbiome Project (HMP) has announced first genomic compilation of the generalized biome of microbes in the human body that complement the human genome. In a sprawling series of coordinated scientific reports published on June 14, 2012, in *Nature* and several journals in the Public Library of Science (PLoS), some 200 members of the HMP Consortium from nearly 80 multidisciplinary research institutions report on five years of research. HMP received \$153 million from the NIH Common Fund, a trans-NIH initiative that finances high-impact, large-scale research.

"Like 15th century explorers describing the outline of a new continent, HMP researchers employed a new technological strategy to comprehensively define, for the first time, the normal microbial makeup of the human body," said NIH Director Francis S. Collins, M.D., Ph.D. "HMP created a remarkable reference database by using genome sequencing techniques to directly detect microbes in healthy volunteers. This lays the foundation for accelerating infectious disease research previously impossible without this community resource."

The human body contains trillions of microorganisms—outnumbering human cells by 10 to one. Because of their small size, however, microorganisms make up only about one to three percent of the body's mass, but play a vital role in human health.

HMP researchers reported that this plethora of microbes contribute more genes responsible for human survival than humans themselves. Where the human genome carries some 22,000 protein-coding genes that carry out metabolic activities, researchers estimate that the microbiome contributes some 8 million unique protein-coding genes or 360-times more bacterial genes than human genes. In addition, the bacterial genomic contribution is critical for human survival. Genes carried by bacteria in the gastro-intestinal track, for example, allow humans to digest foods and absorb nutrients that otherwise would be unavailable.

"Humans don't have all the enzymes we need to digest our own diet," said Lita Proctor, Ph.D., HMP program manager. "Microbes in the gut breakdown much of the proteins, lipids and carbohydrates in our diet into nutrients that we can then absorb. Moreover, the microbes produce beneficial compounds, like vitamins and anti-inflammatories (compounds that suppress inflammation in the gut) that our genome cannot produce."

To define the normal human microbiome, HMP researchers sampled 242 healthy U.S. volunteers (129 male, 113 female), collecting tissues from 15 body sites in men and 18 body sites in women (including three vaginal sites). Researchers collected up to three samples from each volunteer at sites such as the mouth, nose, skin (two behind each ear and each inner elbow), and lower intestine (stool).

Where doctors had previously isolated only a few hundred bacterial species from the body, HMP researchers now calculate that more than 10,000 species occupy the human ecosystem. Moreover, researchers calculate that they have found between 81 and 99 percent of all the genres of microorganisms in healthy adults.

Defining "a" human biome, however, can be difficult, as HMP researchers found immense variation in bacterial communities, both in bacterial diversity and in bacterial group abundances - variation that includes population differences both between areas in each body and between similar areas in different bodies.

Each body site can be inhabited by organisms as different as those in the Amazon Rainforest and the Sahara Desert. Further, these sites on different individuals are populated with different assemblages of bacteria, or with some of the same bacteria, but in markedly different proportions.

In one companion paper, researchers asked the question of whether there were particular types of bacteria that were common, or "core", across all the human subjects in the HMP cohort. Defining a core bacteria as one present in 95% of all subjects, an analysis performed by Sue Huse and colleagues published in *PLoS ONE* ("A Core Human Microbiome as Viewed Through 16S rRNA Sequences Clusters," SM Hulse, Y Ye, Y Zhou, A Fodor) found that the nine sample sites from the mouth had the highest numbers of shared core bacteria, with the number of core varieties shared between stool samples being somewhat lower and very few core bacteria found at the skin and vagina sample sites.

Anthony Fodor, a co-author on the paper and an associate professor in bioinformatics at UNC Charlotte, notes however that, while there are a small core of commonly shared bacteria found at some body sites, he and his colleagues found the abundances of the "core" taxa at the sample sites could vary by several orders of magnitude between individuals.

"Consider stool samples," he said. "There's one sample where a particular type of bacteria represents about 90% of the sequences that we saw. But then there are other samples where it represents not 90% but .01% - and there's everything in between. And this kind of variation is not just true of this type of bacteria but of essentially every type of bacteria within the HMP.

"Since all of the volunteers within the HMP were healthy, this tells us that there do not appear to be particular bacteria that are required to be present in high numbers to maintain health," Fodor noted.

Interestingly, this high level of variation in bacterial populations does not mean that the combined metabolic functions those populations perform are similarly different.

"The microbiome doesn't work that way," Fodor said. "You and I can both be perfectly healthy and one taxa can represent 95% of my gut, and be .01% of your gut. Maybe that is explained by the analysis in the Nature paper that shows that even though the types of bacteria are different, the function of genes within the genomes of these different bacteria appear to be very similar." From these data, it appears that different bacteria within the body can perform similar ecological functions, according to Fodor.

"It remains an open question how individual variation in the types of bacteria within healthy people influences disease development," Fodor continued. "It will be really interesting to see how this question is resolved as the field continues to mature and we learn more about the contribution of the microbiome to specific diseases such as obesity, cancer, fatty liver and inflammatory bowel disease."

[http://www.eurekalert.org/pub\\_releases/2012-06/uoc--fai061312.php](http://www.eurekalert.org/pub_releases/2012-06/uoc--fai061312.php)

### **Folic acid intake during early pregnancy associated with reduced risk of autism in offspring**

***A study suggests that women who consume the recommended daily dosage of folic acid during the first month of pregnancy may have a reduced risk of having a child with autism.***

SACRAMENTO, Calif. - A new study by researchers at the UC Davis MIND Institute suggests that women who consume the recommended daily dosage of folic acid, the synthetic form of folate or vitamin B-9, during the first month of pregnancy may have a reduced risk of having a child with autism.

The study furthers the researchers' earlier investigations, which found that women who take prenatal vitamins around the time of conception have a reduced risk of having a child with autism. The current study sought to determine whether the folic acid consumed in those supplements was the source of the protective effect. The finding suggests that, in addition to women who already have conceived, those who are attempting to become pregnant should consider consuming folic acid supplements, the authors said.

The study found that women who each day consumed the recommended amount of folic acid (600 micrograms, or .6 milligrams) during the first month of pregnancy experienced a reduced risk of having a child with autism spectrum disorder, specifically when the mother and/or her child had a specific genetic variant (MTHFR 677 C>T) associated with less efficient folate metabolism. The study will be published in the July issue of the American Journal of Clinical Nutrition.

"This research is congruent with the findings of earlier studies that suggest that improved neurodevelopmental outcomes are associated with folic acid intake in early pregnancy," said lead study author Rebecca J. Schmidt, assistant professor of public health sciences in the UC Davis School of Medicine and a researcher with the UC Davis MIND Institute. "It further supports recommendations that women with any chance of becoming pregnant should consider consuming folic acid at levels of 600 micrograms or greater per day."

Autism is a neurodevelopmental disorder characterized by impairments in social interaction, communication deficits and repetitive behaviors and often is accompanied by intellectual disability. An estimated 1 in 88 children born today will be diagnosed with autism spectrum disorder, according to the U.S. Centers for Disease Control and Prevention.

"What's reassuring here is knowing that, by taking specific action in terms of their intake of folic acid from food or supplements, women can reduce the risk of autism spectrum disorder in their future children," said study senior author Irva Hertz-Picciotto, chief of the division of environmental and occupational health in the Department of Public Health Sciences and a MIND Institute researcher.

The study authors said that folic acid offers protection against problems in embryonic brain development by facilitating DNA methylation reactions that can lead to changes in the way that the genetic code is read. An



ample supply of methyl donors such as folic acid could be especially important in the period around conception, when the DNA methylation road map is set forth.

For the study, the researchers collected data from approximately 835 Northern California mothers of 2- to 5-year-old children who had autism, developmental delay or typical development and who were participants in the Childhood Autism Risk from Genetics and the Environment (CHARGE) study between 2003 and 2009. Each mother's average daily folic acid intake was assessed on the basis of the amount and the frequency of consumption of folic acid-containing dietary supplements such as prenatal vitamins and multivitamins, as well as the consumption of food supplemented with folic acid such as fortified breakfast cereals or energy bars. Information was collected for the period when the women were pregnant and for the three months before they became pregnant.

The study found that mothers of typically developing children reported greater-than-average intake of folic acid, and were more likely to meet intake recommendations during the first month of pregnancy than were mothers of children with autism spectrum disorder. Among study participants, as the amount of folic acid consumed increased, the associated risk for autism spectrum disorder decreased. Mothers of children with developmental delay tended to have lower estimated folic acid intake when compared with mothers of typically developing children during the three months before pregnancy.

The mothers of infants who were developing normally said they consumed an average 779 micrograms of folic acid daily and 69 percent of them at least met the daily guidelines. The mothers of children with autism consumed an average of 655 micrograms of folic acid. Fifty-four percent of them consumed the recommended 600 micrograms or more per day

Consuming supplemental folic acid before and during early pregnancy has been recommended for decades, after studies demonstrated its potential to prevent up to 70 percent of neural tube defects, or improper formation of the embryonic brain and spinal cord. Folic acid's protective effect on neural tube defects also was stronger when mothers and/or children carried the MTHFR 677 C>T gene variant. Early maternal folic acid supplementation has more recently been shown to improve other social, attention and behavioral outcomes in the developing child.

*Additional study authors include Daniel J. Tancredi, Sally Ozonoff, Robin Hansen, Linda Schmidt and Flora Tassone of UC Davis and Jaana Hartiala and Hooman Allayee of the University of Southern California.*

*The study was funded by grants from the National Institutes of Health for both the CHARGE Study and this work (1R01-ES015359, 5R01-ES015359-03S1, P01-ES11269, 2K12HD051958-06, and T32-MH073124) and by grants R-829388 and R833292 from the U.S. Environmental Protection Agency's Science to Achieve Results (STAR) program and the UC Davis MIND Institute.*

[http://www.eurekalert.org/pub\\_releases/2012-06/hf-esl061312.php](http://www.eurekalert.org/pub_releases/2012-06/hf-esl061312.php)

## **Epileptic seizures linked to common childhood viral infection**

### ***Could antiviral treatment prevent some cases of epilepsy?***

SANTA BARBARA, CA - A ten-year NIH-funded study has determined that a third of infants with prolonged seizures and fever suffer from either a new or reactivated roseola virus infection. Roseola viruses are the cause of the common childhood rash, but can also cause limbic encephalitis, a condition that frequently progresses to epilepsy. Investigators discovered one of the roseola viruses, human herpesvirus-6B (HHV-6B) in the blood of 32% of 169 infants with prolonged seizures, a condition known as status epilepticus. They found HHV-7 (another roseola virus) in 7.1% of the patients, usually as a co-infection with HHV-6B.

The study strengthens the link between HHV-6B and mesial temporal lobe epilepsy. HHV-6B is the primary cause of limbic encephalitis in transplant patients and half of those cases go on to develop epilepsy within 3-5 years. Furthermore, several studies have found HHV-6B DNA at high levels in the brain tissue of patients with refractory epilepsy. "A clinical trial is urgently needed to determine if repeat seizures and some cases of temporal lobe epilepsy might be prevented using existing antiviral therapy," said Kristin Loomis, executive director of the HHV-6 Foundation.

These viruses persist in the brain cells and can be activated during periods of immunosuppression or stress. HHV-6 and HHV-7 are spread via the saliva and nearly 100% of the population has been infected by early adulthood.

### **Do childhood viruses smolder and emerge later as full-blown epilepsy?**

"It is possible that these patients harbor latent virus in the brain tissue that reactivates later in response to unknown triggers," said Leon Epstein, MD, a pediatric neurologist at the Northwestern University Feinberg School of Medicine and Ann & Robert H. Lurie Children's Hospital of Chicago. Dr. Epstein is the lead author of this new study published in the journal *Epilepsia*.

While febrile or fever-related seizures occur in 2-5% of infants, most of whom recover with no consequences, less is known about the outcome in children who suffer from the prolonged febrile seizures associated with HHV-6 or HHV-7. These children are still being followed and investigators expect that 30-40% of them will develop epilepsy within five years.

### **Would some infants with prolonged seizures benefit from antiviral treatment?**

Currently infants with seizures are not tested for HHV-6B or HHV-7 and treatment consists of anti-seizure drugs. However, the authors expect clinical trials to be established as soon as more evidence is gathered. Transplant patients suffering with seizures from HHV-6 reactivation are routinely treated with antivirals and antiviral treatment is now common practice for symptomatic infants infected with a closely related virus: cytomegalovirus or CMV (HHV-5). Infants who contract CMV from their mothers during pregnancy or shortly following birth can develop seizures and mental retardation as well as permanent losses in both hearing and vision. Antiviral therapy reduces neurological complications and seizures in these infants. The neurologists who conducted the study remain cautious about antiviral therapy. They note that the oral antiviral drug used to treat CMV infections, valganciclovir, can cause reversible neutropenia, a form of anemia; less toxic antivirals such as CMX001 are in the pipeline.

"HHV-6B can cause a strong cytokine response, and there is emerging data that inflammatory mechanisms may be involved in developing epilepsy after an insult such as a prolonged seizure," explained, Shlomo Shinnar, MD, PhD, of Montefiore Medical Center and Albert Einstein College of Medicine, and principal investigator of the study, "So it is possible that anti-inflammatory treatment could benefit these patients whether or not HHV-6B is the cause of the prolonged seizure. This is an area that needs further research.

### **HHV-6B reactivation associated with cognitive impairment**

Investigators will also be studying the roseola virus subset to determine if they develop cognitive problems in the years following the seizures. "We know that children and adults with temporal lobe epilepsy have cognitive problems. It will be interesting to see whether those who started out with an HHV-6B infection have more cognitive impairment down the road," said Shinnar.

A study by Danielle Zerr, an infectious disease specialist at Seattle Children's Hospital and the University of Washington, suggests that Shinnar may be on the right track. She reported last year that patients who reactivate with HHV-6B during a transplant procedure are far more likely to develop cognitive dysfunction or delirium. The declines were especially significant in areas of attention, processing speed, and concentration, as well as cognitive flexibility or the ability to operate with divided attention.

Children who develop seizures in response to these common viruses may harbor genes that cause them to be susceptible. A mutation in the SCN1A gene has been linked to several epilepsy conditions. Variants of another gene, IRF5, have been associated with active HHV-6A infections in multiple sclerosis patients.

*NINDS: [http://www.ninds.nih.gov/disorders/febrile\\_seizures/detail\\_febrile\\_seizures.htm](http://www.ninds.nih.gov/disorders/febrile_seizures/detail_febrile_seizures.htm)*

*Bien 2007: "Limbic Encephalitis as a precipitating event in adult onset temporal lobe epilepsy"*

*Dunin-Wasocicz 2010: "Successful antiepileptic drug withdrawal in infants with epilepsy and cytomegalovirus neuroinfection: Longitudinal study"*

*Hill 2012: "Cord-blood hematopoietic stem-cell transplantation confers an increased risk for human herpesvirus-6-associated acute limbic encephalitis: a cohort analysis"*

*Suzuki 2007: "Epilepsy in patients with congenital cytomegalovirus infection"*

*Oliver 2012: "Neurodevelopmental outcomes following ganciclovir therapy in symptomatic congenital cytomegalovirus infections involving the central nervous system"*

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*Zerr 2011: "HHV-6 reactivation and its effect on delirium and cognitive functioning in hematopoietic cell transplant recipients"*

<http://news.discovery.com/tech/retinal-prosthesis-120613.html#mkcpgn=rssnws1>

### **Retinal Prosthesis Could Help The Blind See**

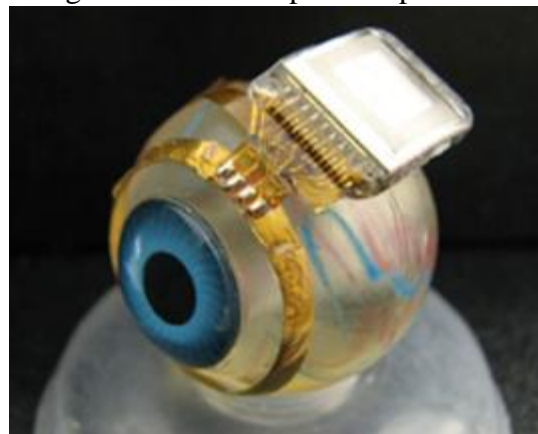
***A retinal implant has given a brief glimpse of light to a small number of blind people, and could one day be a common treatment for vision loss due to injury or disease.***

**Analysis by Jesse Emspak**

Shawn Kelly, a senior systems scientist at Carnegie Mellon University, has developed a computer chip that translates camera images into electrical pulses that the nerves inside the brain can understand. The result is vision.

The cameras are incredibly small and mounted to a pair of glasses. The digital information picked up from the camera is sent along a wire to a thin film surgically implanted in the back of the patient's eye, between the sclera and the retina. The electrical signals stimulate the nerves in the retina, and that allows the patient to see. The system is powered via induction -- not much current is necessary since the electric field doesn't have to penetrate far into the head.

It's a far cry from the bionic eyes of science fiction, though. The resolution is only 256 pixels total, because that's how many electrodes can be made to fit on the back of the film. A typical digital camera has resolutions measured in millions of pixels and ordinary human vision involves approximately 1 million nerves, and more than 100 million rod and cone cells. But it is something.



*Implant\_closeup\_300x258 Image: Carnegie Mellon University*

"At 256 we start to get some function back to people," Kelly told Discovery News. He said people who tested the system reported the ability to see some shapes and light and dark regions. The tests were not "field tests" in real-world conditions, but situations where the implant was used for a few hours and then removed.

There have been other proposals for retinal implants. Recent work in Britain used a self-powered retinal implant that is powered by light that enters the eye rather than the external glasses. At the University of Tubingen in Germany, another project involves an implant that has a 1,500 pixel resolution that is inserted below the retina.

Kelly said the difference with his design is that the processor is sealed well enough that no water vapor gets inside. Ordinarily the liquids in the eye (and the body generally) are in chemical equilibrium, but any implanted device with wires has spaces in it that can allow small amounts of vapor to form, which can reduce the implant's effectiveness." We have more intelligence in the eye," Kelly said. "Ours is designed to be stable long term."

One kind of blindness that will be targeted with this device is retinitis pigmentosa, a hereditary disease that destroys the cells in the eye that receive light. Military veterans could also be helped. (Kelly recently received a \$1.1 million grant from the Department of Veterans' affairs). Some veterans of World War II and Korea suffer from age-related macular degeneration. Others had their eyes damaged by laser rangefinders, Kelly said. The lasers (which are far more powerful than barcode scanners or CD players) can injure the eyes in a way that causes damage later in life.

<http://www.sciencedaily.com/releases/2012/06/120613102132.htm>

### **If Your Dog Is Aggressive, Maybe It Is in Pain**

***The pain produced by hip dysplasia is a key factor in the risk of large dogs becoming aggressive.***

ScienceDaily - Dogs can sometimes suffer sudden episodes of aggression without their owners understanding why. But, in many cases, the cause of these attacks can be pain that has never been diagnosed or treated. For the first time the study describes the characteristics of this irritability, which can make dogs violent and increase aggression in already conflictive individuals.

There are many factors that explain aggression in dogs: the conditions of the mother during gestation, the handling of the puppy in the neonatal phase, the age at weaning, the experiences of the animal during the socialising phase, diet, exercise, genetics and learning techniques based on active punishment during adulthood. However, aggressive behaviour also arises from the presence of pathologies and pain in the dog.

Between 2010 and 2011 a team of researchers from the department of Animal and Food Science at the Autonomous University of Barcelona (UAB) in Spain analysed the aggression problems of 12 dogs (Giant schnauzer, Irish setter, Pit-bull, Dalmatian, two German shepherds, Neapolitan Mastiff, Shih-tzu, Bobtail, Catalan Sheepdog, Chow-chow and Doberman) who were brought to the UAB's Veterinary Hospital by their owners.

"All (eleven males and one female) were diagnosed as having aggression caused by pain. Out of the 12 studied, eight had suffered a hip dysplasia," as was outlined by Tomás Camps, lead author of the study that was published in the Journal of Veterinary Behavior and researcher at the Animal Nutrition and Welfare Service of the UAB.

Scientists identified the most frequent circumstances in which dogs were aggressive, the most characteristic positions, the most frequent target of attacks and if they were impulsive or, in other words, whether or not they showed signs before an imminent attack.

The study shows that dogs that were already aggressive for other reasons before the onset of pain attacked their owners more intensely and frequently when food was taken away, when they were moved from their rest area or when they were made to do something. Animals displayed aggression in the same situations (or nearly) as those that were already aggressive.

On the other hand, "dogs that had never been aggressive before the onset of pain began to behave in this way in situations where an attempt is made to control them," points out Camps.

In addition, the study shows that those dogs were more impulsive or, in other words, attacked with no prior warning in the form of growls, for instance. The research team states that "if the pet is handled when in pain, it will quickly act aggressively to avoid more discomfort without the owner being able to prevent it."

### **Diagnosing hip dysplasia**

Canine hip dysplasia affects more than 40% of Golden Retrievers, Labradors and Rottweillers and is a hereditary and degenerative bone disorder that affects the joint connecting the hip and the femoral head. In general, it can affect any breed of large dog but is less frequent in small breeds.

The new study suggests that the pain produced by hip dysplasia is a key factor in the risk of large dogs becoming aggressive. But the problem begins when the dog experiences periods of little pain and the illness is not diagnosed on time. The researchers have reassessed the importance of diagnosis and treatment of pain since, according to Camps, "it can cause aggression or worsen aggression problems."

*Tomás Camps, Marta Amat, Valentina M. Mariotti, Susana Le Brech, Xavier Manteca. Pain-related aggression in dogs: 12 clinical cases. Journal of Veterinary Behavior: Clinical Applications and Research, 2012; 7 (2): 99 DOI: 10.1016/j.jveb.2011.08.002*

<http://www.sciencedaily.com/releases/2012/06/120613102426.htm>

### **Research Punctures 'Modern' Fathers Myth -- Except for Diapers, That Is 'Modern' fathers have been around for far longer than we think, but they have only recently started to change diapers**

ScienceDaily - 'Modern' fathers have been around for far longer than we think, but they have only recently started to change diapers according to research from the University of Warwick.

In a new paper published on the History & Policy website June 13, Dr Laura King from the University of Warwick's Centre for the History of Medicine said the assumption that fathers have only become more involved in looking after their children over the past 20 years is not true. However, statistics show it has taken longer for dads to get to grips with dirty diapers. Figures from a 1982 study showed 43% of fathers never changed a diaper. By 2000 another study showed this figure had fallen to 3%. A 2010 study by the National Perinatal Epidemiology Unit reported that 65% of men helped 'a great deal' with diaper changing.

Dr King has looked at archive material including newspapers, social research and interviews with fathers. She said: "We must reject suggestions that close father-child relationships have only developed since the 1970s or even 1990s. The stereotype of the distant and tyrannical Victorian patriarch conceals substantial evidence of fathers who cared greatly for their children and played with them, educated them, and even nursed them."

The study suggests that in the post Second World War era, fathers were more determined to cultivate much closer relationships with their children than they had experienced with their own fathers.

This was reinforced by important social trends, the reduction in average family size meant that many parents could devote more time to each of their children. A decrease in working hours and increased holiday time also meant that men had more time available to spend with their families. Dr King said there was an emphasis on the nuclear family after 1945 caused by the expansion of state welfare and psychological thinking about the family. She said: "We have to rethink this idea that 'modern' fathers are a recent phenomenon. Such stereotypes affect policy-making and the way legislation is used; fathers are still subject to harmful stereotyping. There is a great deal of historical evidence showing that fathers have played a caring and nurturing role with their children for centuries, including taking informal paternity leave to support their partners around the time of childbirth. However, it does seem to have taken a while for the majority of fathers to take their turn in changing dirty diapers.

"By 1982 there were still 43% of fathers who never changed a nappy [diaper]. This figure has dropped to 3% by 2000. We can see from the 2010 figures that more men are changing nappies on a regular basis. Whilst we can point to clear practical changes such as nappy-changing, men's participation in childbirth, policy changes introducing official paternity leave and changes in child custody laws, the change in active fatherhood has been less sudden than is often assumed."

*'Supporting Active Fatherhood in Britain', Dr Laura King, is available at: <http://www.historyandpolicy.org/papers/policy-paper-132.html>. Dr King's research is currently supported by the Wellcome Trust, and was previously supported by the AHRC.*

## **Earth Worlds Common, Pre-Earth ETs Possible**

***Earth-sized planets may be widespread in the Milky Way, since they don't need metal-rich parent stars to form, suggests new analysis of data from NASA's planet-hunting Kepler space telescope.***

**Irene Klotz**

Planets up to about four times the diameter of Earth form under a broader range of environmental conditions than gas giant planets, the analysis shows.

Scientists looked at 152 stars hosting planets or suspected planets that are Neptune-sized or smaller. They found that small planets, unlike gas giants, don't need metal-rich parent stars to form.

"Our analysis based on the Kepler planet candidates indicates that terrestrial planets can form at a wide range of metallicities, including metallicities almost four times lower than that of the sun," wrote lead author Lars Buchhave, with the Niels Bohr Institute at the University of Copenhagen.

The study, published this week in *Nature*, has several interesting implications. For one, since so-called metal-poor stars -- those made of just hydrogen and helium -- developed before metal-rich ones, planets around these stars (which formed from the same raw materials as their parent stars) didn't have the right stuff for life, at least life as we know it.

"The elements from which planets and our bodies are made did not exist," Yale University astronomer Debra Fischer noted in a related *Nature* paper. But knowing that the formation of rocky planets can occur in lower-metal environments than those of gas giants lowers the bar for what it takes to create an Earth-like world, since they can form around a bigger range of stars, so it may have been easier for earths and Earth-like life to form.

"There could be some places in the universe where rocky planets and life got an earlier start than did Earthlings," Fischer wrote.

<http://bit.ly/Lxb1iJ>

## **Milk fats clue to inflammatory bowel disease**

***Concentrated milk fats, a common ingredient of processed foods and confectionary, trigger blooms of otherwise rare gut bacteria in mice that may contribute to inflammatory gut diseases.***

**18:00 13 June 2012 by Andy Coghlan**

The discovery coincides with release this week of the "microbiome" – the most comprehensive census yet of the species of bacteria that live in and on the human body. By providing an inventory of bugs that live in 18 sites on the body in healthy people, the Human Microbiome Project should enable researchers to explore how disease might result from perturbations to the microbes, similar to those observed in the mice fed milk fat. Eugene Chang at the University of Chicago and colleagues gave mice milk fat, lard or safflower oil to see how it would alter the spectrum of bugs living in the gut. The mice were genetically engineered to mimic inflammatory bowel disease, unable to make a protein called interleukin 10 which normally damps down inflammation.

To their surprise, the researchers found that in mice fed the milk fat, *Bifidobacterium wadsworthia* – bacteria that are normally extremely rare – became much more common, rapidly multiplying from practically zero to 6 per cent of the species found in the gut. The bacteria produce substances that irritate the gut lining and make it more porous, admitting immune cells that trigger inflammation.

Milk fats are hard to break down, requiring much higher-than-usual concentrations of sulphur-rich bile from the liver. Because *B. wadsworthia* makes its energy by consuming sulphur-rich food, it thrived.

"We're hoping to use this information to prevent or treat this disease," says Chang. "We can hopefully re-shape the gut microbiome to make it healthier," he says.

### **Dietary change?**

"The *wadsworthia* bacteria survived only in the mice eating the milk fat," says another member of the team, Suzanne Devkota, also at Chicago. "When we stopped feeding them milk fats, the bacteria disappeared," she said.

Chang says the finding tallies with other studies which found that *B. wadsworthia* thrives when people have blood poisoning, a burst appendix or abscesses. He thinks that the bacteria might trigger inflammatory bowel disease, but that other factors take over and sustain it once the disease has been initiated.

It is too early to say whether avoiding milk fats would help alleviate or prevent the disease in people, though.

"First, we want to study humans to see if they respond in a similar way to the mice to these diets," says Chang. Meanwhile, the origins of many diseases may become clearer thanks to the first comprehensive census of the entire human microbiome, reported in two papers in *Nature* and 12 papers in the open-access PLoS journals, as well as a collection of papers in last week's *Science*.

The investigators who produced the papers catalogued the bacterial species that colonised 18 different sites in the human body, using samples from 242 healthy individuals aged 18 to 40 in the US.

"Knowing which microbes live in various ecological niches in healthy people allows us to better investigate what goes awry in diseases thought to have a microbial link, like Crohn's disease and obesity," says George Weinstock, associate director of the Genome Institute at Washington University in St Louis and one of the Human Microbiome Project's principal investigators.

They found that microbial cells outnumber native human cells by 10 to one, and collectively have 8 million genes compared to just 22,000 in humans. Of the 10,000 species identified, the most diverse range lived on the skin. Bacteria that colonise the teeth are different from those in saliva, and the vagina hosts the simplest range of bugs.

Among the many new insights, researchers found that bacterial populations in the vagina change when a woman is pregnant. Another team discovered that the range of microbial species growing in different parts of the body is probably dictated by the nutrients produced there through normal bodily functions.

*Journal references: Nature, DOI: 10.1038/nature11225*

[http://www.eurekalert.org/pub\\_releases/2012-06/nyph-hvi061412.php](http://www.eurekalert.org/pub_releases/2012-06/nyph-hvi061412.php)

### **Hidden vitamin in milk yields remarkable health benefits**

***Weill Cornell researchers show tiny vitamin in milk, in high doses, makes mice leaner, faster and stronger***

NEW YORK - A novel form of vitamin B3 found in milk in small quantities produces remarkable health benefits in mice when high doses are administered, according to a new study conducted by researchers at Weill Cornell Medical College and the Polytechnic School in Lausanne, Switzerland.

The findings, recently reported in the June 2012 issue of the journal, *Cell Metabolism*, reveal that high doses of the vitamin precursor, nicotinamide riboside (NR) — a cousin of niacin — prevent obesity in mice that are fed a fatty diet, and also increase muscle performance, improve energy expenditure and prevent diabetes development, all without side effects.

The Swiss researchers, led by Dr. Johan Auwerx, performed the mouse experiments, while the ability to give the animals sufficient doses of NR was made possible by Weill Cornell Medical College researchers, who played key roles in uncovering the biological story of NR.

"This study is very important. It shows that in animals, the use of NR offers the health benefits of a low-calorie diet and exercise — without doing either one," says Dr. Anthony Sauve, associate professor of Pharmacology at Weill Cornell Medical College.

Dr. Sauve is the pharmacologist and organic chemist who has invented a simple method for efficiently synthesizing NR in large scale. He was first to show that NR increases nicotinamide adenine dinucleotide (NAD) levels in mammalian cells. NAD is a central player in energy metabolism. He has pioneered research into the compound, and he is a leader in investigating how NAD can signal adaptation in cells and in physiology.

"The research also suggests that the effects of NR could be even broader," Dr. Sauve says. "The bottom line is that NR improves the function of mitochondria, the cell's energy factories. Mitochondrial decline is the hallmark of many diseases associated with aging, such as cancer and neurodegeneration, and NR supplementation boosts mitochondrial functioning."

The Swiss researchers call NR a "hidden vitamin" that is believed to also be present in many other foods, although levels are low and difficult to measure. Nevertheless, the effects of NR on metabolism "are nothing short of astonishing."

#### **Got nicotinamide riboside?**

The study depended on a series of crucial discoveries by Dr. Sauve and his laboratory colleagues.

NR, related to niacin and other common forms of vitamin B3, was first investigated more than 60 years ago by a Stanford researcher and 1959 Nobel Laureate, Arthur Kornberg. But little more was known about its effects in mammals until Dr. Sauve discovered the effect NR had in stimulating levels of NAD in mammalian cells — work he published in 2007.

NAD allows sugars, fats, and proteins to be converted into energy. Dr. Sauve's research provided the first evidence that NR enhances NAD levels in the mitochondria in mammalian cells in culture. These findings are published in the current study. These cell-based observations were key to the demonstration that NR could stimulate tissue NAD levels in animals, and that it could stimulate NAD-dependent sirtuins, which adapt physiology to the low calorie diets that are known to extend the lifespan of many organisms.

Dr. Sauve invented a relatively simple method for efficiently synthesizing NR in large scale so that its health benefits can be studied. This methodology, which makes it possible to make NR commercially available, was patented by Cornell's Center for Technology Enterprise and Commercialization and subsequently licensed to ChromaDex Corporation.

The development of a means to synthesize NR in adequate quantities was crucial to the current research, and the Sauve lab provided methods and NR to make the study possible. In addition, the biological observations on the effects of NR on NAD levels in cells and on mitochondria were key to the study. Finally, the Sauve laboratory has developed state of the art analytical methods to determine NAD levels in cells, tissues and organelles, and the laboratory provided several key metabolic measurements highlighted in the study.

"Our published scientific work has verified that NR is perhaps the most potent NAD enhancing agent ever identified," he says. His laboratory is also widely recognized for developing an expertise in the measurement of NAD metabolism in cell tissues.

With this compound, the Swiss researchers found that mice on a high-fat diet supplemented with NR gained significantly less weight (60 percent) than mice fed the same diet without NR, even though the mice supplemented with NR ate the same amount of food as mice on the high fat diet not treated with NR. They had improved energy. They were in better shape than the untreated mice, with significantly better endurance and stronger muscles. Additionally, none of the treated mice developed diabetes, as seen in the untreated mice on the high fat diet. And when fed a normal diet, NR treated mice had improved sensitivity to insulin. The NR treated mice also showed lower cholesterol levels. All of these benefits came without toxicity.

While the new study demonstrates that high doses of NR can largely prevent the negative health consequences of a poor diet in mice, Dr. Sauve stresses that the effects of high doses of the vitamin in humans have not been evaluated. "It is important to keep in mind that the amount of NR in milk and other foods appears to be small. We don't know what effects NR would have in humans at relatively high doses," he says.

"Still, we have very encouraging evidence of benefits of NR and NAD augmentation in general from this animal study — and much more work to do," he says.

*The study's senior investigator Dr. Auwerx is head of Laboratory of Integrative Systems Physiology at the Polytechnic School in Lausanne (École Polytechnique Fédérale de Lausanne or EPFL) and the first author is Dr. Carles Cantó, also of EPFL. Other co-authors include Dou Y. Youn and Dr. Yana Cen from Weill Cornell Medical College; Dr. Riekelt H. Houtkooper, Dr. Eija Pirinen, Dr. Maaïke H. Oosterveer, Dr. Pablo J. Fernandez-Marcos, Dr. Hiroyasu Yamamoto, Dr. Pénélope A. Andreux, Dr. Philippe Cettour-Rose, Dr. Kristina Schoonjans and Dr. Chris Rinsch from EPFL; Dr. Karl Gademann from the University of Basel in Switzerland.*

*The Ellison Medical Foundation New Scholar Award and the New York State Spinal Cord Injury Board funded study contributions by the Weill Cornell Medical College researchers.*

<http://www.sciencedaily.com/releases/2012/06/120613133032.htm>

## **Where Humans Split from Sharks: Common Ancestor Comes Into Focus** ***The common ancestor of all jawed vertebrates on Earth resembled a shark***

ScienceDaily - The common ancestor of all jawed vertebrates on Earth resembled a shark, according to a new analysis of the braincase of a 290-million-year-old fossil fish that has long puzzled paleontologists.

New research on *Acanthodes bronni*, a fish from the Paleozoic era, sheds light on the evolution of the earliest jawed vertebrates and offers a new glimpse of the last common ancestor before the split between the earliest sharks and the first bony fishes -- the lineage that would eventually include human beings.

"Unexpectedly, *Acanthodes* turns out to be the best view we have of conditions in the last



*These are various latex molds taken from the fossil of *Acanthodes bronni*. (Credit: Megan Doherty/University of Chicago)*

common ancestor of bony fishes and sharks," said Michael Coates, PhD, professor of organismal biology and anatomy at the University of Chicago and senior author of the study published in *Nature*. "Our work is telling us that the earliest bony fishes looked pretty much like sharks, and not vice versa. What we might think of as shark space is, in fact, general modern jawed vertebrate space."

The group gnathostomes, meaning "jaw-mouths," includes tens of thousands of living vertebrate species, ranging from fish and sharks to birds, reptiles, mammals and humans. Cartilaginous fish, which today include sharks, rays, and ratfish, diverged from the bony fishes more than 420 million years ago. But little is known about what the last common ancestor of humans, manta rays and great white sharks looked like. Coates and colleagues Samuel Davis and John Finarelli found answers to this mystery in an unexpected place: the acanthodians, extinct fishes that generally left behind only tiny scales and elaborate suites of fin spines. But armed with new data on what the earliest sharks and bony fishes looked like, Coates and colleagues re-examined fossils of *Acanthodes bronni*, the best-preserved acanthodian species. Davis created highly detailed latex molds of specimens revealing the inside and outside of the skull, providing a valuable new data set for assessing cranial and jaw anatomy as well as the organizations of sensory, circulatory and respiratory systems in the species.

"We want to explore braincases if possible, because they are exceptionally rich sources of anatomical information," Coates said. "They're much better than scales, teeth or fin spines, which, on their own, tend to deliver a confusing signal of evolutionary relationships." The analysis of the sample combined with recent CT scans of skulls from early sharks and bony fishes led the researchers to a surprising reassessment of what *Acanthodes bronni* tells us about the history of jawed vertebrates.

"For the first time, we could look inside the head of *Acanthodes*, and describe it within this whole new context," Coates said. "The more we looked at it, the more similarities we found with sharks."

However, analysis of the evolutionary relationships of *Acanthodes bronni* -- even with these new data added -- still connected this species to early bony fishes. Meanwhile, some acanthodian species turned out to be primitive sharks, while others were relatives of the common ancestor of sharks and bony fishes.

This result explains some of the longstanding confusion about the placement of acanthodians in vertebrate history. But additional analyses went a step further. Using more than 100 morphological characters, the researchers quantified the mutual resemblance among the earliest jawed fishes. Acanthodians as a whole, including the earliest members of humans' own deep evolutionary past, appear to cluster with ancient sharks.

"The common ancestors of all jawed vertebrates today organized their heads in a way that resembled sharks," said Finarelli, PhD, Lecturer in Vertebrate Biology at University College Dublin. "Given what we now know about the interrelatedness of early fishes, these results tell us that while sharks retained these features, bony fishes moved away from such conditions." Furthermore, the analysis demonstrated that all of these early members of the modern gnathostomes are clearly separated from what now appear to be the most primitive vertebrates with jaws: a collection of armored fishes called placoderms. "There appears to be a fundamental distinction between the placoderms and all other vertebrates with jaws," Finarelli said.

This new revision of the lineage of early jawed vertebrates will allow paleontologists to dig into deeper mysteries, including how the body plan of these ancient species transformed over the transition from jawless to jawed fishes. "It helps to answer the basic question of what's primitive about a shark," Coates said. "And, at last, we're getting a better handle on primitive conditions for jawed vertebrates as a whole."

"This study is an example of the power of phylogenetics combined with the comparative morphology of living and fossil organisms," said Maureen Kearney, program director in National Science Foundation's Division of Environmental Biology, which co-funded the research. "It shows us important evolutionary transitions in the history of life, providing a new window into the sequence of evolutionary changes during early vertebrate evolution." The study, "*Acanthodes* and shark-like conditions in the last common ancestor of modern gnathostomes," will be published on June 14 by Nature. The research was also funded by the Natural Environment Research Council.

*Samuel P. Davis, John A. Finarelli, Michael I. Coates. Acanthodes and shark-like conditions in the last common ancestor of modern gnathostomes. Nature, 2012; 486 (7402): 247 DOI: 10.1038/nature11080*

<http://www.bbc.co.uk/news/health-18423285>

### **'Hitchhiking' anti-cancer viruses ride blood cells**

***A tumour-killing virus can sneak around the body by "hitchhiking" on the back of blood cells, researchers have shown.***

**By James Gallagher Health and science reporter, BBC News**

It is hoped reoviruses can be used to treat cancer, but there were fears they would not work if the immune system could wipe them out. A study published in Science Translational Medicine showed the viruses could hide in the blood and reach their target. Experts said it was an important step in advancing cancer therapies. Reoviruses are normally harmless, but they can cause stomach upsets and colds in childhood. However, it seems they have the ability to infect and kill some cancerous cells while leaving the surrounding tissue



unharmful. However, experiments on mice suggested the virus would not survive in the blood as the immune system would destroy it. It meant the virus would need to be injected directly into the tumour or be given with drugs to suppress the immune system.

### **Stealth mode**

A study in 10 people at the University of Leeds and The Institute of Cancer Research, at the Royal Marsden Hospital, showed that the virus could escape the immune system by hiding in the blood. All the patients had advanced bowel cancer which had spread to the liver, and were injected with doses of the reovirus ahead of their scheduled surgery.

The virus was detected in the tumour, but not the liver, meaning it was selectively targeting the cancer. In the blood, the virus was detected in blood cells, not the liquid blood plasma all the cells float in, meaning it was "hitchhiking", the researchers said.

Prof Alan Melcher, from the University of Leeds, said the virus was "even cleverer" than previously thought. "By piggybacking on blood cells, the virus is managing to hide from the body's natural immune response and reach its target intact." He told the BBC he had "no doubt" the virus would be eventually used "in combination with chemotherapy".

### **'Important next step'**

Dr Kevin Harrington, from the Institute of Cancer Research, said: "Viral treatments like reovirus are showing real promise in patient trials. "This study gives us the very good news that it should be possible to deliver these treatments with a simple injection into the bloodstream."

Why reoviruses affect only cancer cells is not entirely understood. Cancer cells behave very differently to healthy cells, which may make them more susceptible to infection.

Doctors are already testing the virus in some trials in people, such as studies on head and neck cancer.

Prof John Bell, from the University of Ottawa, has researched using genetically modified viruses to attack cancer cells. He said viruses could be "exquisitely selective" in targeting tumours, and that this latest study had shown how safe the technique was. "This study is an important next step in advancing oncolytic virus therapies into cancer patients."

<http://www.bbc.co.uk/news/health-18428265>

### **'Stop opposing assisted dying' - BMJ**

***The British Medical Journal has called on doctors' organisations to stop opposing assisted dying for terminally ill, mentally competent adults.***

In an editorial the BMJ said it wanted the British Medical Association and royal colleges to move their position from opposition to neutrality.

Fiona Godlee, BMJ editor-in-chief, argued that "legalisation is a decision for society not doctors" and drew parallels with abortion legalisation in the 1960s which was initially opposed by medical bodies.

She said: "A change in the law, with all the necessary safeguards, is an almost inevitable consequence of the societal move towards greater individual autonomy and patient choice. But it may take a while, and it may not happen until we properly value death as one of life's central events and learn to see bad deaths in the same damning light as botched abortions."

The BMJ said it backed calls from the campaign group Healthcare Professionals for Assisted Dying (HPAD) which wanted medical bodies to be neutral on the issue.

Iona Heath, president of the Royal College of General Practitioners, wrote in the BMJ last month that the "apparently burgeoning enthusiasm" for assisted dying seemed surprising given recent history. This included "the involvement of doctors in state sponsored killings, personified by Josef Mengele, and the devastating private enterprise of Harold Shipman".

She said it would be impossible to draft a law robust enough to protect the sick and disabled, adding: "A malign government coming into power with legislation supporting assisted dying already in place is a deeply disturbing prospect. As individuals, very few of us act always in the interests of others and, because of this very basic truth, the legalisation of assisted dying, despite the very best of intentions, may render the most vulnerable even more so."

A BMA spokesperson said the organisation was "firmly opposed" to the legalisation of assisted dying adding: "If assisted dying was legalised, effective safeguards could not be implemented without the involvement of doctors. It is therefore appropriate for doctors to voice their views on this issue."

The BMA annual meeting later this month will debate several motions urging neutrality on the issue of assisted dying.

<http://www.bbc.co.uk/news/health-18428889>

## **Ten-year-old girl gets vein grown from her stem cells**

***A 10-year-old girl has had a major blood vessel in her body replaced with one grown with her own stem cells, Swedish doctors report.***

**By James Gallagher Health and science reporter, BBC News**

She had poor blood flow between her intestines and liver. A vein was taken from a dead man, stripped of its own cells and then bathed in stem cells from the girl, according to a study published in the Lancet.

Surgeons said there was a "striking" improvement in her quality of life.

This is the latest in a series of body parts grown, or engineered, to match the tissue of the patient. Last year, scientists created a synthetic windpipe and then coated it with a patient's stem cells.

### **Home-grown**

A blockage in the major blood vessel linking the intestines and the liver can cause serious health problems including internal bleeding and even death. In this case, other options such as using artificial grafts to bypass the blockage, had failed.

Doctors at the University of Gothenburg and Sahlgrenska University Hospital tried to make a vein out of the patient's own cells. It used a process known as "decellularisation". It starts with a donor vein which is then effectively put through a washing machine in which repeated cycles of enzymes and detergents break down and wash away the person's cells. It leaves behind a scaffold. This is then bathed in stem cells from the 10-year-old's bone marrow. The end product is a vein made from the girl's own cells.

The doctors said: "The new stem-cell derived graft resulted not only in good blood flow rates, but also in strikingly improved quality of life for the patient."

Profs Martin Birchall and George Hamilton, from University College London, said: "The young girl was spared the trauma of having veins harvested from the deep neck or leg with the associated risk of lower limb disorders." They said this one-off procedure needed "to be converted into full clinical trials... if regenerative medicine solutions are to become widely used".

[http://www.eurekalert.org/pub\\_releases/2012-06/fiot-sdm061212.php](http://www.eurekalert.org/pub_releases/2012-06/fiot-sdm061212.php)

## **Scientists dispel myths, provide new insight into human impact on pre-Columbian Amazon River Basin**

***A paper published this week in Science provides the most nuanced view to date of the small, shifting human populations in much of the Amazon before the arrival of Europeans.***

MELBOURNE, FLA. - The research, which includes the first landscape-scale sampling of central and western Amazonia, finds that early inhabitants were concentrated near rivers and lakes but actually had little long-term impact on the outlying forests, as if they merely tiptoed around the land far from natural sources of water. In doing so, the new study overturns the currently popular idea that the Amazon was a cultural parkland in pre-Columbian times.

The Amazon Basin is one of Earth's areas of highest biodiversity. Therefore, understanding how Amazonia was modified by humans in the past is important for conservation and understanding the ecological processes of tropical rainforests. Researchers at Florida Institute of Technology, the Smithsonian Institution, Wake Forest University and the University of Florida looked at how widespread human impacts were in Amazonia before the Europeans arrived. If the Pre-Columbian Amazon was a highly altered landscape, then most of the Amazon's current biodiversity could have come from human effects.

The research team, led by Florida Tech's Crystal McMichael and Mark Bush, retrieved 247 soil cores from 55 locations throughout the central and western Amazon, sampling sites that were likely disturbed by humans, like river banks and areas known from archeological evidence to have been occupied by people. They also collected cores farther away from rivers, where human impacts were unknown and used markers in the cores to track the histories of fire, vegetation and human alterations of the soil. The eastern Amazon has already been studied in detail.

McMichael, Bush, and their colleagues conclude that people in the central and western Amazon generally lived in small groups, with larger populations on some rivers. "There is strong evidence of large settlements in eastern Amazonia, but our data point to different cultural adaptations in the central and western Amazon, which left vast areas with very little human imprint," said Bush.

They did not live in large settlements throughout the basin as was previously thought. Even sites of supposedly large settlements did not show evidence of high population densities and large-scale agriculture. All the signs point to smaller, mobile populations before Europeans arrived. The impacts of these small populations were largely limited to river banks.

"The amazing biodiversity of the Amazon is not a byproduct of past human disturbance," said McMichael. "We also can't assume that these forests will be resilient to disturbance, because many have never been disturbed, or have only been lightly disturbed in the past."

Certainly there is no parallel in western Amazonia for the scale of modern disturbance that accompanies industrial agriculture, road construction, and the synergies of those disturbances with climate change."

<http://phys.org/news/2012-06-cougars-re-populating-historical-range.html>

**Cougars are re-populating their historical range, new study confirms**  
***American mountain lions, or cougars, are re-emerging in areas of the United States, reversing 100 years of decline.***

The evidence, published in The Journal of Wildlife Management, raises new conservation questions, such as how humans can live alongside the returning predators.

"The cougar population declined dramatically from 1900, due to both hunting, and a lack of prey, leaving the remaining population isolated to the American west," said Michelle LaRue from the University of Minnesota. "Here we present the hard evidence that the western population has spread, with cougar populations re-establishing across the Midwest."

Three main cougar populations exist in the Midwest centered around The Black Hills in South Dakota, however, cougars are venturing far outside of this range. One male cougar from the Black Hills was found to have traveled 2,900 kilometers through Minnesota, Wisconsin and New York, before ending up in Connecticut.

"While the distance the Connecticut cougar traveled was rare, we found that cougars are roaming long distances and are moving back into portions of their historical range across the Midwest", said LaRue. "Our study took in over 3,200,000 Km<sup>2</sup> of territory, confirming the presence of Cougars from Texas, Arkansas and Nebraska, to the Canadian provinces of Ontario and Manitoba."

Working alongside scientists from Southern Illinois University Carbondale and The Cougar Network, LaRue and Principal Investigator Dr. Clay Nielsen analyzed cougar sightings which have been reported since the 1990's to characterize confirmed sightings over time, assess habitat suitability and confirm where cougar populations are being re-established.

Aside from confirmed sightings, the team's evidence included carcasses, tracks, photos, video, DNA evidence and cases of attacks on livestock across 14 states and provinces of North America. Only sightings which were verified by wildlife professionals were included, while sightings of animals known to be released from captivity were excluded to ensure only natural repopulation was analyzed.

The results reveal 178 cougar confirmations in the Midwest with the number of confirmations steadily increasing between 1990 and 2008. Approximately 62% of confirmed sightings took place within 20km of habitat that would be considered suitable for cougar populations.

When cougar carcasses were recovered 76% were found to be male. As the Connecticut example shows, males are capable of traveling long distances and this finding suggests males are leading a stepping-stone dispersal of the cougar population.

"This evidence helps to confirm that cougars are re-colonizing their historical range and reveals that sightings have increased over the past two decades," concluded LaRue. "The question now is how the public will respond after living without large carnivores for a century. We believe public awareness campaigns and conservation strategies are required across these states, such as the Mountain Lion response plans already in place in Nebraska and Missouri."

*More information: LaRue. M, Nielsen. C, Dowling. M, Miller. K, Wilson. B, Shaw. H, Anderson. C, 'Cougars Are Recolonizing the Midwest: Analysis of Cougar Confirmations during 1990–2008,' Journal of Wildlife Management, Wiley-Blackwell, June 2012, DOI: 10.1002/jwmg.396*

<http://bit.ly/KEgE3T>

**You may carry cells from siblings, aunts and uncles**  
***YOUR siblings may be closer to you than you thought.***  
**14 June 2012 by Linda Geddes**

Male cells have been found in the umbilical cord blood of baby girls with older brothers, suggesting that the transfer of cells between mother and baby may be more extensive than previously imagined. Indeed, all of us may be walking chimeras.

Previous studies have shown that cells from both mother and fetus can cross the placenta during pregnancy, and survive for decades in the skin, liver, brain and spleen - a phenomenon called fetal microchimerism. There is even evidence that fetal cells may repair damage to the mother's heart during pregnancy.

Other studies have hinted that fetal cells might contribute to autoimmune disease, prompting speculation that fetal cells disperse more widely, possibly passing between siblings and even across generations. To investigate this, Miranda Dierselhuis of Leiden University Medical Center in the Netherlands and her colleagues analysed umbilical cord blood from 23 newborn girls, 17 of whom had older brothers. In a subset of the samples, they looked for immune cells directed against the male Y chromosome.

Of the 12 girls in the subset with elder brothers, 11 had cord blood containing immune cells against the Y chromosome, suggesting that male cells had somehow crossed the placenta from the mother - presumably entering her body from a male fetus during an earlier pregnancy. In some of the girls, DNA testing revealed direct evidence of male cells in the cord blood (Blood, DOI: 10.1182/blood-2012-02-410571).

"We may be more microchimeric than we imagined," says Dierselhuis, although she cautions that they haven't yet confirmed the source of the male cells.

Curiously, small numbers of male cells were also detected in one of the girls with no older brother, raising the possibility that these cells were from her uncle, passing to her mother during her grandmother's pregnancy. Another possibility is that they originated from an earlier miscarriage of which the mother was unaware.

"It shows just how ubiquitous the exchange of these cells is," says Hilary Gammill of the Fred Hutchinson Cancer Research Center in Seattle. "We used to think of the placenta as a complete barrier."

Last year, Gammill detected cells in the blood of pregnant women that came from their mothers - the grandmother of their fetus. The number of the cells increased as the pregnancies progressed (PLoS One, DOI: 10.1371/journal.pone.0024101).

"We think the mother's cells shape the ability of the developing immune system to learn tolerance," Gammill says. "We wonder if the grandmother's cells are continuing that education process in some way."

The discovery of even wider transfer of cells between siblings and across generations raises the possibility that these cells may influence the course of health or disease in all of us. Several diseases including asthma, type 1 diabetes and certain cancers are less common in younger siblings. "Even in small numbers, some of these cells have stem-like properties, so I think they could influence health," says Gammill.

Meanwhile, an autoimmune disease called scleroderma - which causes hardening of the skin and blood vessels - has also been linked to the presence of fetal cells in the blood, and seems to be more common in younger siblings. "The further you are down the line in birth order, the greater the risk," says Maureen Mayes at the University of Texas in Houston, who has studied the phenomenon (Arthritis Care and Research, DOI: 10.1002/acr.20096). "Multi-fetal microchimerism is one possible explanation," she says.

And Christoph Bucher of the University of Minnesota in Minneapolis reported in 2007 that stem-cell transplants from cord blood between siblings for various types of blood disease appeared to be more successful if the cells came from younger siblings. This hints that a level of tolerance had already developed between donor's and receiver's cells (Blood, DOI: 10.1182/blood-2007-02-076257). Previously it was assumed that cord blood was immunologically naive, but Dierselhuis's study may help to explain this phenomenon.

However, Bucher is cautious about whether the new study will have any immediate clinical impact. "It's a fascinating idea but it's not something that could be exploited clinically at this stage," he says. "More detailed studies are needed to show conclusively that sibling A is in the cord blood of sibling B."

<http://www.scientificamerican.com/article.cfm?id=nanomedicine-penetrates-vaginal-mucus>

### **Small Comfort: Nanomedicine Able to Penetrate Bodily Defenses**

***Researchers use stealthy nanoscale particles to infiltrate vaginal mucus and keep herpes at bay in mice***

**By Larry Greenemeier | June 14, 2012 | 2**

Tears and a runny nose can be unpleasant on a windy day, but these mucosal secretions play a vital role in protecting the body from viruses and other malicious microbes. Unfortunately, mucus is also adept at washing away medication designed to treat infections and inflammation that occur when an infectious agent is successful in penetrating the body's defenses

Knowing that even nanoscale particles of medicine are apt to get caught up in layers of mucus and cleared before they can treat an ailment, a team of Johns Hopkins University scientists has developed specially coated nanoparticles that can penetrate deep into the body's defenses and remain long enough to kill harmful microbes. More specifically, the researchers broke down the herpes-fighting drug acyclovir into nanosize units coated with low-molecular weight polyethylene glycol (PEG) and applied them to female mice using a vaginal gel. The PEG-coated acyclovir particles—about 110 nanometers in size, only slightly larger than a virus—penetrated the cervicovaginal mouse mucus and remained in the vaginal folds there for 24 hours. Less than half of the mice receiving this treatment were infected with herpes simplex virus, whereas 84 percent of mice given

the same concentration of acyclovir using uncoated nanoparticles were infected, the researchers reported Wednesday in Science Translational Medicine.

This is the first time the researchers can report a successful nanomedical herpes treatment in living animals, says Justin Hanes, a project researcher and director of the Center for Nanomedicine at the Johns Hopkins University School of Medicine. One of the places where microbicides fail is that they do not fully cover vaginal tissue because the vagina is an organ that has deep folds known as rugae enabling it to expand during childbirth or intercourse, says Hanes, also a co-founder of Kala Pharmaceuticals—a Waltham, Mass.–based company he formed with Massachusetts Institute of Technology Institute Professor Robert Langer to develop mucus-penetrating nanoparticles for treating diseases in the eyes and lungs.

In the reproductive, respiratory and gastrointestinal tracts as well as the sinuses the body clears mucus layers every few minutes. "We needed to design a system that, like some viruses capable of infecting humans at mucosal surfaces, would allow treatment to penetrate deep into the mucus layer where they would not be cleared as rapidly by the body," Hanes says. "Our goal was to coat and line the epithelium with particles [of acyclovir] and then have them stay there with a uniform distribution and release the drug over a longer period of time than you'd have if you administered the treatment in a standard gel preparation that uses uncoated nanoparticles."

"The use of a nanoscale delivery vehicle with [this type of] surface functionality is key to this advance," says Paula Hammond, a chemical engineering professor at M.I.T. Hammond, who did not participate in the Johns Hopkins research, is studying ways to use what she refers to as PEG-coated "stealth" nanoparticles to penetrate and treat cancerous tumors. "The [Johns Hopkins] work shows the relevance of nanomedicine not only for treatment of diseases such as cancer, but for a breadth of other medical applications."

Indeed, Hanes and his colleagues are already targeting their stealthy nanoparticles at several other areas, including eye ailments normally treated with medicated drops as well as the delivery of gene therapy for those suffering from cystic fibrosis. "We have grants to study this for a variety of diseases, including lung cancer and cervical cancer," he says. "We're also trying to develop a similar nanoparticle for a good HIV drug known as tenofovir to see if we can make that drug more effective."

<http://phys.org/news/2012-06-hindcasting-scientists-life-earth.html>

### **Hindcasting helps scientists improve forecasts for life on Earth**

***Experts are employing hindcasting – "predicting" what happened during past episodes of climate change – to help them develop and test new models that will improve forecasting***

Earth's changing environment and rapidly growing population are pushing plants and animals out of their native habitats, but current models that predict how this will affect the ecosystem are little more than educated guesses. And when the models have been tested, they've been wildly inaccurate.

A large and diverse group of scientists at the University of California, Berkeley, has launched a unique program, the Berkeley Initiative in Global Change Biology (BiGCB), to improve the reliability and accuracy of these models. The experts are employing hindcasting – "predicting" what happened during past episodes of climate change – to help them develop and test new models that will improve forecasting.

"The only way to test a model and improve forecasting is through hindcasting," said Charles Marshall, director of the University of California Museum of Paleontology and a UC Berkeley professor of integrative biology.

"Once we have a tested model that accurately tells us what is likely to happen to biological systems, we can construct policies to minimize unwanted impacts."

One of the leaders of BiGCB, Marshall said that the university's large museum collections – priceless records of how animals and plants adapted to past ecological change – will allow scientists to travel back in time to study how previous periods of global change, similar to what is now occurring, affected the biosphere. Those data can then be used to test and improve current predictive models and eventually come up with forecasting tools for policy makers and scientists alike.

A recent \$1.5 million grant from the W. M. Keck Foundation will fund the development of a web-based informatics portal that will provide the framework for building the next generation of predictive models, while a new \$2.5 million grant from the Gordon and Betty Moore Foundation will support seven specific projects focused on global change forecasting in California.

"These datasets are pure gold," Marshall said, referring to UC Berkeley's plant, vertebrate, insect and fossil collections.

Information from the museum collections – including the geographic distribution of specimens, their DNA and even hitchhiking pollen and parasites – provides a density of data going back hundreds and, in the case of paleontological collections, millions of years.

According to BiGCB co-leader Rosemary Gillespie, current species distribution models incorporate climate model predictions of how temperature and rainfall will change and assume that an organism will move to areas that match its preferred habitat in terms of temperature, moisture, food and more.

"You might expect that, with warmer temperatures, animals will move up mountains to keep cooler, but we know that it's more complex than that: Some animals are killed off, some adapt to the new conditions, and others move upslope," said Gillespie, a UC Berkeley professor of environmental science, policy and management and director of the campus's Essig Museum of Entomology. "We are hoping to narrow down the parameters that are important in an organism's adaptation to change, and distill those into a model that will be more reliable in predicting how biota and the associated landscape are going to change."

One big difference between the BiGCB and efforts elsewhere is the initiative's focus on a specific ecosystem and every organism in that ecosystem over time in order to develop a complete history of change at that site. The Essig Museum, for example, contains specimens of bees, together with the pollen they were carrying and their parasites, from nearly every year since 1910. New technologies make it possible to use DNA from the historical samples to see how the honey bees, plants, pollination activities and disease have changed in the past, and from that infer how it might change in the future as a result of urbanization or agricultural land conversion. Another BiGCB project involves drilling into Northern California's Clear Lake – one of the oldest lakes in the United States – in search of pollen that will tell how vegetation changed with altered climate as far as 130,000 years into the past. This period covers the last major climate shift in North America, the retreat of glaciers 12,000 years ago. Vegetation changes will be correlated with changes in animal populations as evidenced by fossils collected from numerous caves around Clear Lake and currently held in the Museum of Paleontology. An anthropologist who studies California's Indians will work with pollen experts to correlate human fire use over the past 13,000 years with changes in vegetation at a coastal site near Año Nuevo and the inland area near Pinnacles National Monument.

"UC Berkeley's museums have been involved in collecting species for a long time, and many people asked, 'What use was it?'" Gillespie said. "But with rapid changes now taking place in the environment, the value of that history is roaring to the forefront. With the genomics revolution, we can exploit the collections and see genetic change in action over hundreds of years."

The informatics portal, what BiGCB scientists refer to as the "Keck engine," will combine easily searched, cloud-based databases of museum collections, such as the vertebrate-focused VertNet, with an online visualization tool created at UC Berkeley called Cal-Adapt, which displays a variety of climate change scenarios in map format. The end result could project, for example, how species' ranges will shift in relation to one another, as well as to changes in snow pack, wildfire danger and temperature through the end of the century. "We plan to overlay the collections data on Cal-Adapt data and develop a visual interface that will allow scientists to go backward in time to hindcast as well as forecast," Gillespie said.

"The Keck engine is a really exciting tool, a transformation in how we approach issues of global change," Marshall said. "It should really alter the extent to which we can say if there is a link between global change and biotic change." *Provided by University of California - Berkeley*

<http://www.sciencedaily.com/releases/2012/06/120614131101.htm>

### **New Action for Ancient Heart Drug**

#### ***A drug used for centuries activates the body's own protective mechanisms in blood vessels***

ScienceDaily - University of Michigan Health System study shows a drug used for centuries activates the body's own protective mechanisms in blood vessels. An ancient heart drug that's inspired the work of herbalists and poets for centuries may treat a condition that plagues millions of overstressed and overweight Americans today. Since the 13th century, the herb and poisonous plant Foxglove has been used to cleanse wounds and its dried leaves were carefully brewed by Native Americans to treat leg swelling caused by heart problems.

In an article published online June 14 in *Molecular Pharmacology*, researchers at the University of Michigan Health System reveal that digoxin, the active ingredient in digitalis, or the poisonous plant Foxglove, can enhance the body's own protective mechanism against high blood pressure and heart failure.

High blood pressure can be prevented by reducing salt intake, being active and keeping a healthy weight, but about 1 in 3 Americans has high blood pressure, also called hypertension, which can damage the body in many ways. Most current treatments prevent excess hormone and stress signals that can lead to high blood pressure and heart failure. But recent studies have found that the body has the ability to keep excess stimulation in check through production of a family of inhibitors called RGS proteins.

Researchers looked for ways to "re-purpose" old drugs to tap into this protective mechanism which is lost among some individuals with high blood pressure and heart failure. "We tested several thousand known drugs

and bioactive molecules for a potential role in enhancing RGS2 and/or RGS4 expression and function and have identified a novel mechanism for digoxin," says lead study author Benita Sjogren, Ph.D., a research fellow in the Department of Pharmacology at the University of Michigan.

Case histories collected by Dr. William Withering in 1775 determined that Foxglove contained the active ingredient, digoxin, now an important drug for treating patients with congestive heart failure.

This new action of digoxin was found by treating engineered human kidney cells with thousands of known drugs in a high-throughput screen at the U-M Center for Chemical Genomics. Digoxin was then shown to have similar actions in isolated mouse blood vessel cells.

"In addition to test tube studies, low dose digoxin, the active ingredient of digitalis, was able to increase RGS2 levels in the heart and kidney," says senior study author and pharmacologist Rick Neubig, M.D., Ph.D., professor of pharmacology, associate professor of internal medicine, and co-director of the Center for Chemical Genomics at the University of Michigan. "This new action of digoxin could help explain the fact that low doses seem to improve the survival of heart failure patients. It also suggests new uses for low dose digoxin or other drugs that can activate this protective mechanism," he says.

Neubig's lab at the U-M focuses on the large family of RGS proteins and the role they play in the function of the brain, heart, immunity and cancer and how they can be exploited in therapeutics.

*B. Sjogren, S. Parra, L. J. Heath, K. B. Atkins, Z. Xie, R. Neubig. Cardiotonic Steroids Stabilize RGS2 Protein Levels. Molecular Pharmacology, 2012; DOI: 10.1124/mol.112.079293*

[http://www.eurekalert.org/pub\\_releases/2012-06/uoc--cnm061512.php](http://www.eurekalert.org/pub_releases/2012-06/uoc--cnm061512.php)

### **Cancer's next magic bullet may be magic shotgun**

#### ***Network approach to drug design may yield more effective and less toxic cancer drugs, UCSF study suggests***

A new approach to drug design, pioneered by a group of researchers at the University of California, San Francisco (UCSF) and Mt. Sinai, New York, promises to help identify future drugs to fight cancer and other diseases that will be more effective and have fewer side effects. Rather than seeking to find magic bullets—chemicals that specifically attack one gene or protein involved in one particular part of a disease process—the new approach looks to find "magic shotguns" by sifting through the known universe of chemicals to find the few special molecules that broadly disrupt the whole diseases process.

"We've always been looking for magic bullets," said Kevan Shokat, PhD, a Howard Hughes Medical Institute Investigator and the Chair of the Department of Cellular and Molecular Pharmacology at UCSF. "This is a magic shotgun—it doesn't inhibit one target but a set of targets—and that gives us a much, much better ability to stop the cancer without causing as many side effects."

Described in the June 7, 2012 issue of the journal *Nature*, the magic shotgun approach has already yielded two potential drugs, called AD80 and AD81, which in fruit flies were more effective and less toxic than the drug vandetanib, which was approved by the U.S. Food & Drug Administration last year for the treatment of a certain type of thyroid cancer.

#### **Expanding the Targets to Lower a Drug's Toxicity**

Drug design is basically all about disruption. In any disease, there are numerous molecular interactions and other processes that take place within specific tissues, and in the broadest sense, most drugs are simply chemicals that interfere with the proteins and genes involved in those processes. The better a drug disrupts key parts of a disease process, the more effective it is.

The toxicity of a drug, on the other hand, refers to how it also disrupts other parts of the body's system. Drugs always fall short of perfection in this sense, and all pharmaceuticals have some level of toxicity due to unwanted interactions the drugs have with other molecules in the body.

Scientists use something called the therapeutic index (the ratio of effective dose to toxic dose) as a way of defining how severe the side effects of a given drug would be. Many of the safest drugs on the market have therapeutic indexes that are 20 or higher—meaning that you would have to take 20 times the prescribed dose to suffer severe side effects. any cancer drugs, on the other hand, have a therapeutic index of 1. In other words, the amount of the drug you need to take to treat the cancer is the exact amount that causes severe side effects. The problem, said Shokat, comes down to the fact that cancer drug targets are so similar to normal human proteins that the drugs have widespread effects felt far outside the tumor.

While suffering the side effects of drugs is a reality that many people with cancer bravely face, finding ways of minimizing this toxicity is a big goal pharmaceutical companies would like to solve. Shokat and his colleagues believe the shotgun approach is one way to do this. The dogma that the best drugs are the most selective could be wrong, he said, and for cancer a magic shotgun may be more effective than a magic bullet.

Looking at fruit flies, they found a way to screen compounds to find the few that best disrupt an entire network of interacting genes and proteins. Rather than judging a compound according to how well it inhibits a specific target, they judged as best the compounds that inhibited not only that specific target but disrupted other parts of the network while not interacting with other genes and proteins that would cause toxic side effects.

*The article, "Chemical genetic discovery of targets and anti-targets for cancer polypharmacology" by Arvin C. Dar, Tirtha K. Das, Kevan M. Shokat and Ross Cagan appears in the June 7, 2012 issue of the journal Nature. See: <http://dx.doi.org/10.1038/nature11127>*

*This work was supported by the American Cancer Society, The Waxman Foundation, and the National Institutes of Health—through grants R01CA109730, R01CA084309, R01EB001987 and P01 CA081403-11.*

<http://phys.org/news/2012-06-bones-bulgaria-john-baptist.html>

### **Bones in Bulgaria may be of John the Baptist: study**

***Scientists have found new evidence they say supports the theory that a knuckle bone and other human remains found under a church floor in Bulgaria may be of John the Baptist.***

The relics found in a small marble sarcophagus two years ago on a Bulgarian island called Sveti Ivan, which translates as Saint John, also included a human tooth, part of a skull and three animal bones.

A research team from Oxford University dated the right-handed knuckle bone to the first century AD, when John is believed to have lived until his beheading ordered by king Herod, the university said in a statement. And scientists from the University of Copenhagen analysed the DNA of the bones, finding they came from a single individual, probably a man, from a family in the modern-day Middle East, where John would have lived. While these findings do not definitively prove anything, they also don't refute the theory first proffered by the Bulgarian archaeologists who found the remains while excavating under an ancient church on the island. Many sites around the world claim to hold relics of the saint, including the Grand Mosque in Damascus which says it has his head. The right hand with which the prophet allegedly baptised Jesus in the River Jordan is also claimed to be held by several entities, including a Serbian Orthodox monastery in Montenegro.

"The result from the metacarpal hand bone is clearly consistent with someone who lived in the early first century AD," Oxford University professor Tom Higham said of the new study. "Whether that person is John the Baptist is a question that we cannot yet definitely answer and probably never will."

Bulgarian archaeologists had found a small box made of hardened volcanic ash close to the sarcophagus. The box bore inscriptions in ancient Greek that referred to John the Baptist and the date that Christians celebrate his birth, June 24. The findings of another Oxford researcher, using historical documents, suggest that the monastery of Sveti Ivan may have received a portion of John the Baptist's relics in the fifth or early sixth centuries. The findings are to be presented in a documentary to be aired on The National Geographic channel in Britain on Sunday.

<http://www.sciencedaily.com/releases/2012/06/120615141657.htm>

### **New Surgery May Reverse Hand Paralysis**

***"Even if a patient appears to have lost total hand function, as long as there is some nerve in the arm or shoulder under the patient's control, some mobility may be regained"***

ScienceDaily - Justin M. Brown, MD, reconstructive neurosurgeon at UC San Diego Health System, is one of only a few specialists in the world who have pioneered a novel technique to restore hand function in patients with spinal cord injury. In a delicate four-hour procedure, Brown splices together tiny nerve endings, only one millimeter in width, to help restore hand mobility. Most patients return home 24 hours after surgery.

"Even if a patient appears to have lost total hand function, as long as there is some nerve in the arm or shoulder under the patient's control, some mobility may be regained," said Brown, director of the Neurosurgery Peripheral Nerve Program and co-director of the Center for Neurophysiology and Restorative Neurology at UC San Diego Health System. "With a nerve transfer, the goal is to reverse paralysis. This means achieving functional grasp and release so that patients can eat independently, operate a computer or hold a loved one's hand."

Brown and his team treat hand impairments at cervical level 5 and below. Operating under a microscope, Brown disconnects the damaged nerve and reconnects it to a healthy one. The healthy nerve is taken from underneath the muscles of the upper arm and then connected to a nerve branch that provides finger function. In contrast to muscle transfers, nerve transfers allow whole muscle groups to be restored in the arm without visibly changing the body's anatomy. "The nerves grow at a rate of 1 millimeter per day," said Brown, who is also founding member and first president of the International Society for Restorative Neurology. "Over a period of six to 12 months, patients can essentially wake up their arms and hands and return to a satisfying level of functionality and improved quality of life."



Brown said that patients occasionally experience temporary weakness where the original healthy nerve is taken. These muscles, however, can recover their original strength. Casting and immobilization is seldom needed after the surgery. He added that the overall result is that multiple hand functions can be restored with a single transplant. "The recovery of hand function is consistently rated as the highest priority for persons with quadriplegia," said Brown. "While nerve transfers take longer to heal so that axons can regenerate, patients often experience better long-term biomechanical outcomes."

In the United States there are approximately 300,000 people living with spinal cord injuries with 12,000 new injuries occurring each year. More than half of these injuries result in neck-level injuries that lead to loss of hand and arm function. Brown said this technique may also be offered in select cases to patients with paralysis as a result of trauma, stroke, or brain injury.

Brown earned his medical degree from the Eastern Virginia Medical School in Norfolk. He completed a surgical internship and neurosurgical residency at Baylor College of Medicine in Houston and a peripheral nerve fellowship in the Division of Plastic and Reconstructive Surgery at Washington University School of Medicine. He was formerly co-director of the Peripheral Nerve Center at Washington University in St. Louis.

<http://bit.ly/MidvTo>

### **Algorithm beats jigsaw-solving record**

***We have met our match at the genteel pastime of jigsaw puzzles.***

**10:00 16 June 2012 by Jacob Aron**

It seems an algorithm can now whiz through 10,000 pieces in 24 hours. The speedy solver could also help piece together shredded documents or archaeological artefacts. Andrew Gallagher at Cornell University in Ithaca, New York, wrote the algorithm while working at photography firm Kodak. By mimicking the way a human solves jigsaws, it beat last year's record of 3300 pieces. The algorithm can even solve multiple puzzles at the same time, where the pieces have been mixed up together.

Unlike other software that only analyses the edges of the pieces, Gallagher's looks at how colour patterns spread across many pieces. For example, if one piece becomes progressively lighter from left to right, it is likely that the piece nestles between a lighter piece on the left and a darker one on the right.

The algorithm only works on jigsaws with square pieces, which are harder to solve because the shape offers no clues. The algorithm calculates a score for each pair, stores the best matches, and uses these to assemble the whole puzzle.

It starts with the two pieces that match best, then the next two and so on, but crucially these matches don't have to be adjacent, allowing the algorithm to work on multiple parts of the puzzle at once. Previous methods worked only on a single part, making it harder to spot when it is going wrong. The system will be presented at the computer vision and pattern recognition conference in Providence, Rhode Island, later this month.

#### **Shredder challenge**

In addition to solving puzzles, Gallagher also used elements of his algorithm to enter last year's DARPA Shredder Challenge, in which participants had to piece together a series of shredded documents. Gallagher's attempt came in at 17 overall – he says because the puzzle pieces in the challenge were digital images of shredded documents made it harder for the algorithm, as the jagged edges did not line up perfectly and some pieces were missing.

Ohad Ben-Shahar, a computer scientist at Ben-Gurion University in Beer-Sheva, Israel, whose team holds the previous puzzle-solving record, says that Gallagher's algorithm is impressive because it can handle puzzles in which the orientation of the pieces is unknown, a more challenging problem.

In terms of performance, Ben-Shahar says their algorithm can match Gallagher's, although they haven't yet published the results, but both algorithms could probably be improved. "With little effort, the time to solution could drop significantly below a day."

<http://bit.ly/LnRExt>

### **Gut bugs confined to quarters by special immune cells**

***Trillions of gut bacteria important for our health are prevented from escaping to other tissues by special immune cells.***

**10:00 17 June 2012 by Andy Coghlan**

There is a fine line between help and harm. The trillions of gut bacteria that are important for our health are prevented from escaping to cause havoc in other tissues by special immune cells.

A team led by David Artis at the University of Pennsylvania School of Medicine in Philadelphia has demonstrated, using mice, that the immune cells – innate lymphoid cells – confine bacteria to the gut by barricading the lining of the gut and neighbouring tissues. Keeping the microbes in check seems to be

important: other research has shown that they are abnormally abundant in the blood of people with Crohn's disease.

When the team eliminated the innate lymphoid cells from mice, the bacteria escaped to other parts of the body. The immune cells work by secreting a chemical called interleukin-22. Treatment with IL-22 provided an effective alternative to the immune cells.

### **Border collies**

It is possible that the immune system has evolved several subsets of cells to shepherd specific groups of gut bacteria. "It may be that the immune system is more sophisticated in controlling these bacteria than we thought," says Artis. The discovery opens up new ways to treat diseases aggravated by bugs that escape from the gut, says Lora Hooper of the University of Texas Southwestern Medical Center in Dallas.

"This work has uncovered some truly exciting new insights into the role of innate lymphoid cells in the gut, showing that they function like border collies that keep intestinal bacteria from escaping to other parts of the body," she says. *Journal reference: Science, DOI: 10.1126/science.1222551*

[http://www.eurekalert.org/pub\\_releases/2012-06/asfm-tmc061312.php](http://www.eurekalert.org/pub_releases/2012-06/asfm-tmc061312.php)

### **The most contaminated surfaces in hotel rooms**

***An experiment of surfaces in hotel rooms finds television remotes to be among the most heavily contaminated with bacteria and items on housekeeping carts carry the potential to cross-contaminate rooms.***

Researchers from the University of Houston report the findings today at the 2012 General Meeting of the American Society for Microbiology. "Hoteliers have an obligation to provide their guests with a safe and secure environment. Currently, housekeeping practices vary across brands and properties with little or no standardization industry wide. The current validation method for hotel room cleanliness is a visual assessment, which has been shown to be ineffective in measuring levels of sanitation," says Katie Kirsch an undergraduate student at the University of Houston who presented the study.

As the public becomes increasingly concerned with public health, hotel room cleanliness and sanitation are becoming consideration factors for consumers when selecting a hotel room. Contact with contaminated surfaces is a possible mode of transmission of illness during outbreaks in hotels. This, combined with the lack of standardization of hotel room cleanliness, poses a risk for hotel guests, specifically immunocompromised individuals who are more susceptible to infection.

"Currently, housekeepers clean 14-16 rooms per 8-hour shift, spending approximately 30 minutes on each room. Identifying high-risk items within a hotel room would allow housekeeping managers to strategically design cleaning practices and allocate time to efficiently reduce the potential health risks posed by microbial contamination in hotel rooms," says Kirsch.

The study was designed as the first step in applying the Hazard Analysis and Critical Control Points (HACCP) system to hotel room cleanliness. Originally developed by the National Aeronautics and Space Administration, HACCP is a systematic preventive approach that identifies potential physical, chemical and biological hazards and designs measurements to reduce these risks to safe levels. Kirsch and her colleagues at the University of Houston, along with researchers from Purdue University and the University of South Carolina sampled a variety of surfaces from hotel rooms in Texas, Indiana and South Carolina. They tested the levels of total aerobic bacteria and coliform (fecal) bacterial contamination on each of the surfaces.

While some of the most contaminated samples, including the toilet and the bathroom sink, were to be expected, they also found high levels of bacterial contamination on the TV remote and the bedside lamp switch. Most concerning, some of highest levels of contamination were found in items from the housekeepers' carts, including sponges and mops which pose a risk for cross-contamination of rooms. Surfaces with the lowest contamination included the headboard on the bed, curtain rods and the bathroom door handle. The researchers cannot say whether or not the bacteria detected can cause disease, however, the contamination levels are a reliable indicator of overall cleanliness.

Kirsch warns that this study is preliminary and is limited by the sample size, which included only 3 rooms in each state and 19 surfaces within each hotel room, but hopes that it is just the beginning of a body of research that could offer a scientific basis to hotel housekeeping.

"The information derived from this study could aid hotels in adopting a proactive approach for reducing potential hazards from contact with surfaces within hotel rooms and provide a basis for the development of more effective and efficient housekeeping practices," says Kirsch.

*Katie Kirsch will participate in a live webcast media availability to discuss her research on Sunday, June 17, 2012 at 2:00 p.m. EDT. The webcast can be found online at [www.microbeworld.org/asmlive](http://www.microbeworld.org/asmlive).*

<http://phys.org/news/2012-06-ancient-greened-antarctica.html>

## **Ancient warming greened Antarctica, research finds**

***A new university-led study with NASA participation finds ancient Antarctica was much warmer and wetter than previously suspected.***

Phys.org - The climate was suitable to support substantial vegetation -- including stunted trees -- along the edges of the frozen continent.

The team of scientists involved in the study, published online June 17 in Nature Geoscience, was led by Sarah J. Feakins of the University of Southern California in Los Angeles, and included researchers from NASA's Jet Propulsion Laboratory in Pasadena, Calif., and Louisiana State University in Baton Rouge.

By examining plant leaf wax remnants in sediment core samples taken from beneath the Ross Ice Shelf, the research team found summer temperatures along the Antarctic coast 15 to 20 million years ago were 20 degrees Fahrenheit (11 degrees Celsius) warmer than today, with temperatures reaching as high as 45 degrees Fahrenheit (7 degrees Celsius). Precipitation levels also were found to be several times higher than today.

"The ultimate goal of the study was to better understand what the future of climate change may look like," said Feakins, an assistant professor of Earth sciences at the USC Dornsife College of Letters, Arts and Sciences.

"Just as history has a lot to teach us about the future, so does past climate. This record shows us how much warmer and wetter it can get around the Antarctic ice sheet as the climate system heats up. This is some of the first evidence of just how much warmer it was."

Scientists began to suspect that high-latitude temperatures during the middle Miocene epoch were warmer than previously believed when co-author Sophie Warny, assistant professor at LSU, discovered large quantities of pollen and algae in sediment cores taken around Antarctica. Fossils of plant life in Antarctica are difficult to come by because the movement of the massive ice sheets covering the landmass grinds and scrapes away the evidence.

"Marine sediment cores are ideal to look for clues of past vegetation, as the fossils deposited are protected from ice sheet advances, but these are technically very difficult to acquire in the Antarctic and require international collaboration," said Warny.

Tipped off by the tiny pollen samples, Feakins opted to look at the remnants of leaf wax taken from sediment cores for clues. Leaf wax acts as a record of climate change by documenting the hydrogen isotope ratios of the water the plant took up while it was alive.

"Ice cores can only go back about one million years," Feakins said. "Sediment cores allow us to go into 'deep time.'"

Based upon a model originally developed to analyze hydrogen isotope ratios in atmospheric water vapor data from NASA's Aura spacecraft, co-author and JPL scientist Jung-Eun Lee created experiments to find out just how much warmer and wetter climate may have been.

"When the planet heats up, the biggest changes are seen toward the poles," Lee said. "The southward movement of rain bands associated with a warmer climate in the high-latitude southern hemisphere made the margins of Antarctica less like a polar desert, and more like present-day Iceland."

The peak of this Antarctic greening occurred during the middle Miocene period, between 16.4 and 15.7 million years ago. This was well after the age of the dinosaurs, which became extinct 64 million years ago. During the Miocene epoch, mostly modern-looking animals roamed Earth, such as three-toed horses, deer, camel and various species of apes. Modern humans did not appear until 200,000 years ago.

Warm conditions during the middle Miocene are thought to be associated with carbon dioxide levels of around 400 to 600 parts per million (ppm). In 2012, carbon dioxide levels have climbed to 393 ppm, the highest they've been in the past several million years. At the current rate of increase, atmospheric carbon dioxide levels are on track to reach middle Miocene levels by the end of this century.

High carbon dioxide levels during the middle Miocene epoch have been documented in other studies through multiple lines of evidence, including the number of microscopic pores on the surface of plant leaves and geochemical evidence from soils and marine organisms.

While none of these 'proxies' is as reliable as the bubbles of gas trapped in ice cores, they are the best evidence available this far back in time. While scientists do not yet know precisely why carbon dioxide was at these levels during the middle Miocene, high carbon dioxide, together with the global warmth documented from many parts of the world and now also from the Antarctic region, appear to coincide during this period in Earth's history.

*More information: Hydrologic cycling over Antarctica during the middle Miocene warming, DOI: 10.1038/ngeo1498*

**Black bears show counting skills on computers**  
***Black bears have demonstrated counting abilities, in a first for the species.***  
**By Matt Bardo Reporter, BBC Nature**

Three captive bears took a series of number-based tests on a touch-screen computer, research published in the journal *Animal Behaviour* showed. They had to choose between two different-sized sets of dots and were rewarded with food for correct answers.

"People don't generally understand them to be as intelligent as they probably are," said Jennifer Vonk, the researcher who led the study.

Although bears have the largest relative brain size of any carnivore, their cognition is not well understood.



*Deep in thought? Bears can "do something analogous to counting", researchers say*

Dr Vonk, an assistant professor in psychology at Oakland University said that the North American black bears were first trained to understand the process and equipment involved in the tests.

"This is the first published work with bears working on a touch screen," she said. "It hasn't been done with any large carnivores."

The experiment then involved presenting the bears with two sets of dots or "arrays".

"Basically we were looking to see if they can understand to choose less or choose more," she said.

They touched the screen to select one or other of the arrays, and were given food if they got the answer right.

One bear was rewarded for touching the screen with a greater number dots, and for the other two bears, a correct answer was an array with a fewer number of dots.

The team wanted to ensure that the animals were not merely estimating magnitude, a skill that has been shown by many animals.

"We're really trying to differentiate between the ability to perceptually discriminate amount from actually quantifying a number of items," explained Dr Vonk.

So the team varied the pattern of the dots and the shaded area on which the arrays were shown, and in some tests the dots were also moving.

"If there's more dots and less area covered - it's a better indication that they actually do something analogous to counting rather than just estimating the amount of something," Dr Vonk said.

Although the study found that bears did better when the size of the area corresponded to the number of dots, they also found that the bears were capable of compensating for an area that was smaller or larger than normal for the number of dots it contained.

"What was important is that we showed that they could work against that in some of the tests," Dr Vonk said.

Black bears in the wild are often solitary, non-social animals, so the results suggested that animals that do not live in a group may have the ability to make number-based judgements.

"This is really the first test of a species that has not evolved to live socially to see if they can individuate items," she said.

"I think we can't really say that they're absolutely counting at this point but it does look like they're attending to the number of items and not just the area."

Similar tests on primate species allowed the scientists to compare the ability of the black bears with non-human primates. For at least one of the bears, they found a pattern that matched.

These results are among the first to show that bears may have cognitive abilities that are equal to primates.

"I've been working for a while with these bears... but simultaneously I was working with a chimpanzee," said Dr Vonk.

"I find that their abilities so far in terms of categorisation and forming more abstract concepts seem quite comparable."

The techniques used to research the bears' skills could be used in the future to look at bear cognition in more depth.

"It really opens up the door to asking all kinds of comparative and cognitive questions with a species that really hasn't been investigated in that way before," she said.