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## Live Birth Predates Dinosaurs

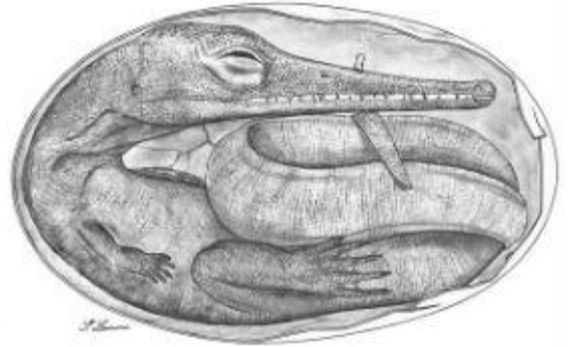
*Despite the fact that the embryos were dated to around 280 million years ago, researchers found them in a remarkably well preserved condition.*

Analysis by Jennifer Viegas

Producing living young, and not external eggs, is a form of birth that could date back to 280 million years ago or even earlier, a new study suggests.

Called viviparity, this form of birth is used by humans, but clearly we were far from being the first to evolve it.

The study, published in the December issue of *Historical Biology: An International Journal of Paleobiology*, focuses on mesosaurs, which were among the world's first aquatic reptiles. They lived in what are now South America and South Africa at a time when these two landmasses were united and part of the giant supercontinent Pangaea.



**Dino-embryo Image: Graciela Piñeiro**

Mesosaurs, and even their earlier ancestors, possibly "were not able to produce hard shelled eggs, at least for the first several million years of their evolution," lead author Graciela Piñeiro, a paleontologist at Uruguay's Facultad de Ciencias, told Discovery News.

"After the recent discovery of mesosaur embryos, we can state with a high degree of confidence that embryo retention developed early in amniote evolution, given that mesosaurs are among the basal-most reptiles and that they date from the Early Permian around 280 million years ago."

Piñeiro and colleagues Jorge Ferigolo, Melitta Meneghel and Michel Laurin recently discovered the exceptionally well-preserved mesosaur embryos at sites in Uruguay and Brazil. The environmental conditions at the locations allowed for the preservation of soft tissues, nerves and blood vessels, she said.

Giving birth in this manner and laying eggs each come with advantages and disadvantages. Eggs with hard, mineralized shells, such as those associated with today's chicken eggs or those of dinosaurs, are believed to help reproduction on dry land. But many terrestrial animals, including humans, do not lay eggs, so there must be other benefits to viviparity.

"We think that the retention of the eggs may have appeared in amniotes as a useful strategy to avoid predation and increase survivorship chances for the embryos," Piñeiro said.

Parental care often then follows. There is even some evidence that mesosaurs provided such care, because adults and juveniles have been associated together in the fossil record.

At least some mesosaurs even had the added challenge of giving birth and raising young in extremely salty water.

"In Uruguay, mesosaurs may have first colonized the shallow water environment of the Mangrullo Formation, which under the establishment of arid climatic conditions that increased evaporation became like a salty marsh where just a few opportunistic organisms could tolerate the anoxic bottom conditions generated by the accumulation of high amounts of organic matter," Piñeiro explained.

When infant mesosaurs entered the world, they possibly even had a salt gland and other anatomical adaptations already in place, allowing them to survive the otherwise challenging conditions.

There is also compelling evidence that giant, carnivorous, four-flipped reptiles known as plesiosaurs gave birth to live young as well. Robin O'Keefe of Marshall University and team discovered a big embryonic marine reptile contained in the fossil of its 15.4-foot-long mother, which lived 78 million years ago.

"The embryo is very large in comparison to the mother," O'Keefe said, "much larger than one would expect in comparison with other reptiles. Many of the animals alive today that give birth to large, single young are social and have maternal care. We speculate that plesiosaurs may have exhibited similar behaviors, making their social lives more similar to those of modern dolphins than other reptiles."

There is one disturbing side-note to such prehistoric potholing: cannibalism.

"Intriguingly, cannibalism is more frequently found in reptiles that are viviparous and develop parental care and social behavior," Piñeiro said.

She and her colleagues are continuing to study viviparity in the fossil record. A paper touching on the connection between mesosaurs and terrestrial animals is forthcoming.

<http://www.sciencedaily.com/releases/2012/12/121210124208.htm>

## **Brown Adipose Tissue Has Beneficial Effects On Metabolism and Glucose Tolerance**

*Brown adipose tissue has beneficial effects on glucose tolerance, body weight and metabolism*

Dec. 10, 2012 - Joslin Diabetes Center scientists have demonstrated that brown adipose tissue (BAT) has beneficial effects on glucose tolerance, body weight and metabolism. The findings, which may lead to new treatments for diabetes, appear in the upcoming issue of the Journal of Clinical Investigation.

Unlike the more prevalent white adipose tissue (WAT or white fat) which stores fat, BAT (or brown fat) burns fat to produce heat. Studies in mice and humans have suggested that BAT also plays a role in regulating body weight and metabolism. This has made BAT the focus of considerable interest among scientists and pharmaceutical companies who are investigating ways to use BAT as a treatment for obesity.

The Joslin researchers were interested in learning whether BAT is involved in glucose metabolism and uncovering the mechanisms underlying BAT's effects on metabolism and body weight. The study involved the transplantation of BAT from male donor mice into the visceral cavities of mice which were fed a standard or high-fat diet.

By eight to twelve weeks following transplantation, the BAT-transplanted mice fed a normal diet showed improved glucose tolerance, increased insulin sensitivity, lower body weights and decreased fat mass. Three control groups, which had a WAT transplant, a glass bead implant or surgery without transplantation, did not show any metabolic improvements. "We were able to establish that BAT transplantation affects metabolism. This study provides further evidence that BAT is a very important metabolic organ and a potential treatment for obesity-related diseases such as diabetes, metabolic syndrome and insulin resistance," says lead author Kristin I. Stanford, PhD, a postdoctoral fellow in the Section on Integrative Physiology and Metabolism.

The mice fed a high-fat diet also exhibited beneficial effects from BAT transplantation, including improved glucose metabolism, decreased body weight and a complete reversal of insulin resistance resulting from excess fat consumption. Previous studies of BAT transplantation in mice, which transplanted BAT in a different location and had a shorter duration, did not show beneficial effects.

The transplanted BAT affected metabolism throughout the body by increasing levels of circulating Interleukin-6 (IL-6). The researchers also found that BAT transplantation increased norepinephrine and FGF-21. IL-6 has been shown in previous studies to increase energy production and decrease body weight. When the researchers transplanted BAT from donor mice genetically engineered not to produce IL-6, the mice who received the transplants showed no metabolic improvements. "This is the first study to demonstrate that an increase in BAT significantly increases levels of circulating IL-6. It suggests that an increase in BAT-derived IL-6 improves glucose metabolism throughout the body," says senior author Laurie J. Goodyear, PhD, head of the Section on Integrative Physiology and Metabolism.

The researchers are following up on the study by "looking into other ways BAT may have beneficial metabolic effects and further investigating the functions of IL-6 and other BAT-derived hormones," says Dr. Goodyear. Dr. Stanford is studying the relationship between BAT and type 1 diabetes (T1D), based on data from a collaborator that suggests that BAT may help control glucose in T1D.

Dr. Goodyear and the research team are very interested in using their findings to develop new therapies for diabetes. "We hope that manipulating BAT will help people with type 1 and type 2 diabetes," says Dr. Goodyear.

Study co-authors include: Roeland J. W. Middelbeek, Kristy L. Townsend, Ding An, Eva B. Nygaard, Kristen M. Hitchcox, Kathleen R. Markan, Kazuhiro Nakano, Michael F. Hirshman, Yu-Hua Tseng, all of Joslin Diabetes Center. *The study was funded by the National Institutes of Health.*

*Kristin I. Stanford, Roeland J.W. Middelbeek, Kristy L. Townsend, Ding An, Eva B. Nygaard, Kristen M. Hitchcox, Kathleen R. Markan, Kazuhiro Nakano, Michael F. Hirshman, Yu-Hua Tseng, Laurie J. Goodyear. Brown adipose tissue regulates glucose homeostasis and insulin sensitivity. Journal of Clinical Investigation, 2012; DOI: 10.1172/JCI62308*

<http://phys.org/news/2012-12-scientists-probe-canadian-sulfide-ore.html>

## **Scientists probe Canadian sulfide ore to confirm microbial activity in seawater 2.7 billion years ago**

*Analysis of sulfide ore deposits from a base-metal mine confirms oxygen levels were extremely low on Earth 2.7 billion years ago, but also shows that microbes were actively feeding on sulfate*

An analysis of sulfide ore deposits from one of the world's richest base-metal mines confirms that oxygen levels were extremely low on Earth 2.7 billion years ago, but also shows that microbes were actively feeding on sulfate in the ocean and influencing seawater chemistry during that geological time period. The research, reported by a team of Canadian and U.S. scientists in Nature Geoscience, provides new insight into how ancient

metal-ore deposits can be used to better understand the chemistry of the ancient oceans – and the early evolution of life.

Sulfate is the second most abundant dissolved ion in the oceans today. It comes from the "rusting" of rocks by atmospheric oxygen, which creates sulfate through chemical reactions with pyrite, the iron sulfide material known as "fool's gold."

The researchers, led by PhD student John Jamieson of the University of Ottawa and Prof. Boswell Wing of McGill, measured the "weight" of sulfur in samples of massive sulfide ore from the Kidd Creek copper-zinc mine in Timmins, Ontario, using a highly sensitive instrument known as a mass spectrometer. The weight is determined by the different amounts of isotopes of sulfur in a sample, and the abundance of different isotopes indicates how much seawater sulfate was incorporated into the massive sulfide ore that formed at the bottom of ancient oceans. That ancient ore is now found on the Earth's surface, and is particularly common in the Canadian shield.

The scientists found that much less sulfate was incorporated into the 2.7 billion-year-old ore at Kidd Creek than is incorporated into similar ore forming at the bottom of oceans today. From these measurements, the researchers were able to model how much sulfate must have been present in the ancient seawater. Their conclusion: sulfate levels were about 350 times lower than in today's ocean. Though they were extremely low, sulfate levels in the ancient ocean still supported an active global population of microbes that use sulfate to gain energy from organic carbon.

"The sulfide ore deposits that we looked at are widespread on Earth, with Canada and Quebec holding the majority of them," says Wing, an associate professor in McGill's Department of Earth and Planetary Science.

"We now have a tool for probing when and where these microbes actually came into global prominence."

"Deep within a copper-zinc mine in northern Ontario that was once a volcanically active ancient seafloor may not be the most intuitive place one would think to look for clues into the conditions in which the earliest microbes thrived over 2.7 billion years ago," Jamieson adds. "However, our increasing understanding of these ancient environments and our abilities to analyze samples to a very high precision has opened the door to further our understanding of the conditions under which life evolved."

More information: [www.nature.com/ngeo/journal/vaop/ncurrent/abs/ngeo1647.html](http://www.nature.com/ngeo/journal/vaop/ncurrent/abs/ngeo1647.html)

<http://www.sciencedaily.com/releases/2012/12/121210133456.htm>

### **Caffeinated Coffee May Reduce the Risk of Oral Cancers**

*People who drank more than four cups of caffeinated coffee per day were at about half the risk of death of often-fatal oral cancers compared to those who only occasionally or who never drank coffee.*

A new American Cancer Society study finds a strong inverse association between caffeinated coffee intake and oral/pharyngeal cancer mortality. The authors say people who drank more than four cups of caffeinated coffee per day were at about half the risk of death of these often fatal cancers compared to those who only occasionally or who never drank coffee. The study is published online in the American Journal of Epidemiology. The authors say more research is needed to elucidate the biologic mechanisms that could be at work.

Previous epidemiologic studies have suggested that coffee intake is associated with reduced risk of oral/pharyngeal cancer. To explore the finding further, researchers examined associations of caffeinated coffee, decaffeinated coffee, and tea intake with fatal oral/pharyngeal cancer in the Cancer Prevention Study II, a prospective U.S. cohort study begun in 1982 by the American Cancer Society.

Among 968,432 men and women who were cancer-free at enrollment, 868 deaths due to oral/pharyngeal cancer occurred during 26 years of follow-up. The researchers found consuming more than four cups of caffeinated coffee per day was associated with a 49 percent lower risk of oral/pharyngeal cancer death relative to no/occasional coffee intake (RR 0.51, 95% confidence interval [CI] 0.40-0.64). A dose-related decline in relative risk was observed with each single cup per day consumed. The association was independent of sex, smoking status, or alcohol use. There was a suggestion of a similar link among those who drank more than two cups per day of decaffeinated coffee, although that finding was only marginally significant. No association was found for tea drinking.

The findings are novel in that they are based specifically upon fatal cases of oral/pharyngeal cancer occurring over a 26-year period in a population of prospectively-followed individuals who were cancer-free at enrollment in Cancer Prevention Study II.

"Coffee is one of the most widely consumed beverages in the world, and contains a variety of antioxidants, polyphenols, and other biologically active compounds that may help to protect against development or progression of cancers," said lead author Janet Hildebrand, MPH. "Although it is less common in the United States, oral/pharyngeal cancer is among the ten most common cancers in the world. Our finding strengthens the

evidence of a possible protective effect of caffeinated coffee in the etiology and/or progression of cancers of the mouth and pharynx. It may be of considerable interest to investigate whether coffee consumption can lead to a better prognosis after oral/pharyngeal cancer diagnosis."

Janet S. Hildebrand, Alpa V. Patel, Marjorie L. McCullough, Mia M. Gaudet, Amy Y. Chen, Richard B. Hayes and Susan M. Gapstur. *Coffee, Tea, and Fatal Oral/Pharyngeal Cancer in a Large Prospective US Cohort. American Journal of Epidemiology*, 2012 DOI: 10.1093/aje/kws222

<http://www.sciencedaily.com/releases/2012/12/121210145234.htm>

### **Most Popular Weight-Loss Drug Strongly Alters Other Drug Therapies, Study Suggests** *The weight-loss drug orlistat, known by the brand names Xenical and Alli, inhibits a key enzyme that may lead to "severe toxicity of internal organs such as the liver and kidney*

A University of Rhode Island researcher has discovered that the weight-loss drug orlistat, known by the brand names Xenical and Alli, inhibits a key enzyme that may lead to "severe toxicity of internal organs such as the liver and kidney." The inhibition is irreversible and can be caused by a low level of the drug.

Professor Bingfang Yan's study funded by the National Institutes of Health, also found that the drug alters efficacy of medicines, and particularly limits the effectiveness of some anti-cancer drugs.

Part of the research results will be published in the journal, *Biochemical Pharmacology*, which has the article posted on its website December 10. Yan also alerted the U.S. Food and Drug Administration to his findings. Orlistat, which was originally approved by the FDA in 1999 as the prescription drug Exenical, was approved in 2007 as the over-the-counter medication Alli. It has been the most commonly used medicine to treat obesity for more than a decade, Yan said. "Since it has been available over-the-counter, there has been a drastic increase of toxicity among patients using the drug," Yan said. "It has been linked to severe liver failure, acute pancreatic failure and acute renal (kidney) failure."

Yan said orlistat works in the intestinal tract by preventing fat from being absorbed by the body. It is generally accepted that orlistat remains in the intestine and that the body does not absorb it.

"But orlistat is reportedly absorbed, and certainly internal organs such as the liver and kidney are exposed to this drug upon absorption," he said. The study showed that the drug is a potent inhibitor of carboxylesterase-2, which is a major detoxification enzyme in the liver, kidney and gastrointestinal track. "When the activity of this enzyme drop in those organs, toxicity increases or the efficacy of some drugs are altered," Yan said.

The enzyme is known to metabolize a wide range of medicines including aspirin and the cancer drugs irinotecan and pentyl carbamate of p-aminobenzyl carbamate of doxazolidine.

"This study shows that orlistat profoundly alters the therapeutic potential of the anti-cancer drugs," Yan said. "In the case of the anti-cancer drugs, it weakens their effectiveness."

Prior or co-presence of orlistat with one of the anti-cancer drugs resulted in cancer cells being far more prolific.

"Alli-based interactions can be key factors in the efficacy of medicines," Yan said. Yan was also interested in Alli's effects on aspirin and its use as a blood thinner. "Aspirin is used to treat blood clots. Yan predicated: "Orlistat would increase the therapeutic potential of aspirin, which may increase the tendency of bleeding."

This isn't the first time that Yan has found critical drug interactions in his studies. In 2006, he discovered that the anti-viral drug Tamiflu would be rendered ineffective in patients also taking the anti-clotting drug Plavix.

His published findings have resulted in new dosing regimens for patients who need both drugs.

Da Xiao, Deshi Shi, Dongfang Yang, Benjamin Barthel, Tad H. Koch, Bingfang Yan. *Carboxylesterase-2 Is A Highly Sensitive Target Of The Antiobesity Agent Orlistat With Profound Implications In The Activation Of Anticancer Prodrugs. Biochemical Pharmacology*, 2012; DOI: 10.1016/j.bcp.2012.11.026

<http://www.sciencedaily.com/releases/2012/12/121210221259.htm>

### **Brain Displays an Intrinsic Mechanism for Fighting Infection**

*Scientists have found that the brain cells of healthy people are likely produce their own immune system molecules*

White blood cells have long reigned as the heroes of the immune system. When an infection strikes, the cells, produced in bone marrow, race through the blood to fight off the pathogen. But new research is emerging that individual organs can also play a role in immune system defense, essentially being their own hero. In a study examining a rare and deadly brain infection, scientists at The Rockefeller University have found that the brain cells of healthy people likely produce their own immune system molecules, demonstrating an "intrinsic immunity" that is crucial for stopping an infection.

Shen-Ying Zhang, a clinical scholar in the St. Giles Laboratory of Human Genetics of Infectious Diseases, has been studying children with Herpes simplex encephalitis, a life-threatening brain infection from the herpes virus, HSV-1, that can cause significant brain damage. The scientists already knew from previous work that children with this encephalitis have a genetic defect that impairs the function of an immune system receptor --



toll-like receptor 3 (TLR3) -- in the brain. For this study they wanted to see how the defect in TLR3 was hampering the brain's ability to fight the herpes infection.

When TLR3 detects a pathogen it triggers an immune response causing the release of proteins called interferons to sound the alarm and "interfere" with the pathogen's replication. It's most commonly associated with white blood cells, found throughout the body, but here the researchers were examining the receptor's presence on neurons and other brain cells.

"One interesting thing about these patients is that they didn't have any of the other, more common herpes symptoms. They didn't have an infection on their skin or their mouths, just in their brains. We therefore hypothesized that the TLR3 response must be specifically responsible for keeping the herpes virus from infecting the brain and not necessary in other parts of the body," says Zhang.

The lab, headed by Jean-Laurent Casanova, collaborated with scientists at Harvard Medical School and Memorial Sloan-Kettering Cancer Institute to create induced pluripotent stem cells. Made from the patients' own tissue, the stem cells were developed into central nervous system cells that carried the patients' genetic defects. Zhang exposed the cells to HSV-1 and to synthetic double-stranded RNA, which mimics a byproduct of the virus that spurs the toll-like receptors into action. By measuring levels of interferon, Zhang showed that the patients' TLR3 response was indeed faulty; their cells weren't making these important immune system proteins, leaving them unable to fight off the infection. Zhang also exposed the patients' blood cells to the virus and found that the TLR3 defect was not an issue there as it was in the brain -- interferons were released by other means.

Because the toll-like receptors on neurons proved to be vital in preventing the encephalitis infection, the researchers concluded that brain cells use it as an in-house mechanism to fight infection, rather than relying on white blood cells. When its function was impaired, patients couldn't get better. "This is evidence of an intrinsic immunity, a newly-discovered function of the immune system," says Zhang. "It's likely that other organs also have their own specific tools for fighting infection." The researchers are putting together a pilot study to test an interferon-based treatment in patients with the encephalitis, believing it will help speed recovery and increase the survival rate when used alongside antiviral drugs. They'll also explore whether the brain displays an intrinsic immunity to other types of viral infection.

*Fabien G. Lafaille, Itai M. Pessach, Shen-Ying Zhang, Michael J. Ciancanelli, Melina Herman, Avinash Abhyankar, Shui-Wang Ying, Sotirios Keros, Peter A. Goldstein, Gustavo Mostoslavsky, Jose Ordovas-Montanes, Emmanuelle Jouanguy, Sabine Plancoulaine, Edmund Tu, Yechiel Elkabetz, Saleh Al-Muhsen, Marc Tardieu, Thorsten M. Schlaeger, George Q. Daley, Laurent Abel, Jean-Laurent Casanova, Lorenz Studer, Luigi D. Notarangelo. Impaired intrinsic immunity to HSV-1 in human iPSC-derived TLR3-deficient CNS cells. Nature, 2012; DOI: 10.1038/nature11583*

[http://www.eurekalert.org/pub\\_releases/2012-12/uol-dot121112.php](http://www.eurekalert.org/pub_releases/2012-12/uol-dot121112.php)

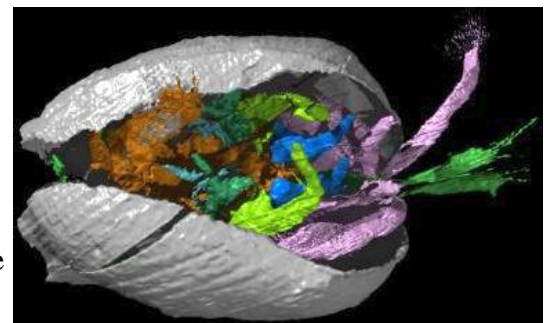
### Discovery of tiny fossil new to science

#### *Rare find from 425 million years ago with body, limbs, eyes, gills and alimentary system preserved*

'It is exciting to discover that a common group of fossils that we thought we knew a lot about may well have been hood-winking us as to their true identity, which we now realise because we have their beautifully fossilised soft-parts. A case of a 'wolf in sheep's clothing' - Professor David Siveter, University of Leicester

An international team of researchers have made an extremely rare discovery of a species of animal - related to crabs, lobsters and shrimps – that is new to science.

Scientists from the universities of Leicester, Oxford, Imperial and Yale have announced their discovery of a new and scientifically important fossil species of ostracod in the journal, Proceedings of The Royal Society B. The research was funded by the Natural Environment Research Council.



*This shows the ventral view of the fossil Pauline avibella.* David J. Siveter, Derek E. G. Briggs, Derek J. Siveter, Mark D. Sutton and Sarah C. Joomun

The discovered species, which is up to 10 millimetres long, is special because it is exceptionally well preserved, complete with not only the shell but also the soft parts – its body, limbs, eyes, gills and alimentary system. Such discoveries are extremely rare in the fossil record.

The discovery of the tiny shelled arthropod was made in 425 million year old rocks in Herefordshire, Welsh Borderland. The rocks at the site date to the Silurian period of geological time, when southern Britain was a sea area on a small continent situated in warm, southerly subtropical latitudes. The ostracods and associated marine animals living there were covered by a fall of volcanic ash that preserved them frozen in time.

Professor David Siveter, of the University of Leicester Department of Geology, said: "The two ostracod specimens discovered represent a genus and species new to science, named *Pauline avibella*. The genus is named in honour of a special person and *avibella* means 'beautiful bird', so-named because of the fancied resemblance of a prominent feature of the shell to the wing of a bird."

"Ostracods are the most abundant fossil arthropods, occurring ubiquitously as bivalved shells in rocks of the last 490 million years, and are common in most water environments today. The find is important because it is one of only a handful preserving the fossilised soft-tissues of ostracods. Its assignment to a particular group of ostracods based on knowledge of its biology is at odds with its shell form, thus urging caution in interpreting the classification of fossil ostracods based on shell characters alone."

"The preservation of soft-parts of animals is a very rare occurrence in the fossil record and allows unparalleled insight into the ancient biology, community structure and evolution of animals - key facts that that would otherwise be lost to science. The fossils known from the Herefordshire site show soft-part preservation and are of global importance."

The fossils were reconstructed 'virtually', by using a technique that involves grinding each specimen down, layer by layer, and photographing it at each stage. Ten millimetres is relatively tiny, but at an incremental level of 20 µm (micrometres) that yields 500 slices, which can then be pieced together in a computer to provide a full, three-dimensional image of each fossil, outside and in.

Professor Siveter added: "Fossil discoveries in general help elucidate our own place in the tree of life. This discovery adds another piece of knowledge in the jigsaw of understanding the diversity and evolution of animals." "It is exciting to discover that a common group of fossils that we thought we knew a lot about may well have been hood-winking us as to their true identity, which we now realise because we have their beautifully fossilised soft-parts. A case of a 'wolf in sheep's clothing'."

The research was undertaken together with Professor Derek Siveter and Dr Sarah Joomun (Oxford), Dr Mark Sutton (Imperial College London) and Professor Derek Briggs (Yale, USA).

*The genus is named in honour of Pauline Siveter, in memoriam, late wife of the lead author of the paper.*

*Siveter DJ, Briggs DEG, Siveter DJ, Sutton MD, Joomun SC. 2012 A Silurian myodocope with preserved soft-parts: cautioning the interpretation of the shell-based ostracod record. Proc R Soc B 20122664.*

[http://www.eurekalert.org/pub\\_releases/2012-12/uoa-wch121112.php](http://www.eurekalert.org/pub_releases/2012-12/uoa-wch121112.php)

### **What causes hot flushes during menopause?**

#### ***A research team has identified a region in the brain that may trigger hot flushes***

Hot flushes are not 'in the head,' but new research suggests they may start there; a UA research team has identified a region in the brain that may trigger the uncomfortable surges of heat most women experience in the first few years of menopause. Hot flushes affect millions of people, and not just women. Yet, it is still unclear what causes the episodes of temperature discomfort, often accompanied by profuse sweating.

Now a team of researchers around Dr. Naomi Rance, a professor in the department of pathology at the UA College of Medicine, has come closer to understanding the mechanism of hot flushes, a necessary step for potential treatment options down the road. This research was published recently in the Proceedings of the National Academy of Sciences.

The team identified a group of brain cells known as KNDy neurons as a likely control switch of hot flushes. KNDy neurons (pronounced "candy") are located in the hypothalamus, a portion of the brain controlling vital functions that also serves as the switchboard between the central nervous system and hormone signals.

"Although the KNDy neurons are a very small population of cells, our research reveals that they play extremely important roles in how the body controls its energy resources, reproduction and temperature," said Melinda Mittelman-Smith, who led the study as part of her doctoral thesis. "They are true multitaskers."

By studying KNDy neurons in rats, the research team created an animal model of menopause to elucidate the biological mechanisms of temperature control in response to withdrawal of the hormone estrogen, the main trigger of the changes that go along with menopause.

They discovered that tail skin temperature was consistently lower in rats whose KNDy neurons were inactivated, suggesting the neurons control a process known as vasodilation, or widening of the blood vessels to increase blood flow through the skin. "The hallmark of hot flushes is vasodilation," explained Rance, who also is a neuropathologist at The University of Arizona Medical Center. "When you flush, your skin gets hot and you can see the redness of the skin. It is an attempt of the body to get rid of heat, just like sweating. Except that if you were to measure core temperature at that point, you would find it is not even elevated."

Although the results are not yet directly applicable in helping individuals affected by hot flushes, they mark a necessary first step, Rance said.

"Obviously we can't do these studies in women, and only if we understand the mechanism is there a chance of developing therapies. All that is known so far is that dwindling estrogen levels have something to do with it but anything after that is a black box." "Right now the only effective way of treating flushes is estrogen-replacement therapy. If we could figure out what is causing those flushes, we could try to develop a better, more targeted therapy." Rance said hot flushes usually last for four or five years and occur in up to 80 percent of women but also in men undergoing certain hormone treatments for prostate cancer. "For some people it's not too bad, but it can be very severe in other individuals; they lose sleep et cetera. So the question I have been asking myself is, 'How come we haven't figured this out?'"

Together with her coworkers, Rance has studied KNDy neurons and their functions for two decades.

"KNDy neurons respond to circulating estrogens," Mittelman-Smith explained. "When these hormones are at very low levels, as is the case in menopause, these neurons go haywire if you will. They grow very large and manufacture several times more neurotransmitter than they did with estrogens present."

"Because the neurons talk to known thermoregulatory centers of the brain, we think this increased signaling activity may inappropriately tell the body, 'I'm hot, release heat.' This triggers heat loss mechanisms like sweating and opening up of blood vessels in the skin."

Analogous to women going through menopause, the tail skin temperature goes up in rats after removal of the ovaries, where estrogen is produced. "Rats regulate heat dissipation with their tail because the rest is covered by fur," Rance explained. "In rats without ovaries, the lack of estrogen causes vasodilation, which we can measure as increased tail skin temperature." "Once we knew that estrogen really does control tail skin temperature in a rat, we wanted to know what role, if any, the KNDy neurons play in this."

When Rance and her team compared the tail skin temperatures of rats with intact KNDy neurons to those with inactivated KNDy neurons, they discovered that while tail skin temperatures still followed the same ups and downs over the course of the day and night cycle, they were lower in the absence of KNDy activity.

"They have lower levels of vasodilation," Rance said. "It is very consistent. Their tail skin temperature is lower than rats with normal KNDy neurons and stays low. It doesn't matter if they have estrogen or not; it doesn't matter if it's night or if it's day."

"The rats didn't seem unhappy at all," she added. "You'd think they'd be curling up and shivering, but no. There was no difference in the core temperature, so they weren't internally cold. We did all the activity measurements and found them to be completely normal. We couldn't tell a difference other than lower vasodilation."

Rance said she is not surprised that the same neuronal switches that are important for reproduction also control thermoregulation. "Being able to regulate body temperature is very important for the species and also for reproduction because it is important for a pregnant woman to avoid extreme hyperthermia. Hot flushes are a symptom of hyperactivity of these neurons."

The researchers caution that while KNDy neurons are critical for normal thermoregulation, they are by no means the sole center for managing body temperature. "These animals would be in much more trouble if that were the case," Mittelman-Smith said. "In fact, I don't view KNDy neurons as a thermoregulatory center at all, but rather a group of cells that has the ability to influence thermoregulatory centers."

Rance added: "I wouldn't say we solved the problem, but we have a good clue about what could be causing the flushes."

*The other members of the research team and authors of the study are: Hemalini Williams, a master's student in the UA's physiology program; Sally Krajewski-Hall, a research associate in Rance's lab; and Nathaniel McMullen, a professor emeritus in the UA's department of cellular and molecular medicine.*

*This work was supported by National Institutes of Health, National Institute on Aging Grant R01 AG032315.*

<http://arstechnica.com/science/2012/12/earths-orbital-cycles-may-trigger-peaks-of-volcanic-eruptions/>

## **Earth's orbital cycles may trigger peaks of volcanic eruptions**

**41,000-year cycle in the Earth's tilt matches up with peak volcanic activity.**

by Scott K. Johnson - Dec 12 2012, 0:35am TST

Over the past couple million years, a rhythmic pattern of climate changes have been driven by cycles in Earth's orbit. These cycles affect the sunlight reaching the Earth, altering seasonal patterns and leading to growing or shrinking ice sheets. The changes echo throughout the Earth, from atmospheric and ocean circulation to ecological responses and even erosion and sediment transport. But could the cycles have affected volcanic eruptions? A new study published in *Geology* argues that they did. Previously, researchers have noticed correlations over limited time periods and regional scales, but the new work extends this to a broader picture, and appears to show a pretty strong link.

To get long records of volcanic eruptions, the researchers used marine sediment cores from around the Pacific Ring of Fire. Unlike on land, where erosion can wash away ash layers, the records in the seafloor sediment



preserve the ash from eruptions that occurred upwind of their location. Errors in the dates assigned to those ashes, which are based on correlating those layers with well-dated ones on land and estimating the rate at which sediment piles up on the seafloor, are difficult to avoid, but the researchers did their best to account for that uncertainty.

After pulling together all the eruptions they identified over the past million years, they analyzed the data for cyclical patterns. They found cycles of the same length as the orbital cycles that affect climate - particularly the 41,000-year cycle in Earth's tilt, which shows up most prominently. To ensure this wasn't a fluke, they artificially generated 100,000 random data sets. Fewer than 1 percent of the data sets contained a signal as strong as the 41,000-year pattern in the actual data.

So why should this be? After all, correlation and causation are very different things. There is a plausible connection here that the researchers explore: stress changes in the Earth's crust caused by glacial cycles. When the climate cools far enough, large ice sheets grow and sea level drops. Those ice sheets actually depress the crust beneath them, which springs back up when the ice melts away. Farther from the ice sheets, great variations in sea level similarly affect the oceanic crust. Raise the sea level, and the oceanic crust gets depressed a bit. Like a squishy, liquid-filled ball (or a balloon), pressing down in one spot causes neighboring areas to bulge outwards. So nearby continental crust (like volcanically active Central and South America) actually pops up a bit when the sea level rises.

If the pressure pushing down on a magma chamber decreases as the crust rebounds upwards, it becomes easier for the magma to work its way to the surface, leading to an eruption. In this way, large climate changes could act to loosen the corks keeping eruptions bottled in, so to speak.

To examine that possibility, the team used a simple computer model that simulated crustal stresses over the last glaciation (or "ice age"). Zooming in on Central America, the eruption record there correlates pretty nicely with periods where the model calculated changing stresses.

Finally, the researchers also looked at the exact timing of the peaks in eruption frequency in relation to the orbital changes. For the 41,000-year tilt cycle, the eruption spikes lag several thousand years behind the changes in tilt (and climate). That makes sense for sluggish crustal responses to changing conditions at the surface - and, in fact, their model simulation behaved similarly.

While the study's eruption data is neither global nor perfectly complete, it seems likely that the group has captured a real pattern. And that pattern once again highlights the interconnectedness of Earth systems - which still hold plenty of surprises. *Geology*, 2012. DOI: 10.1130/G33419.1 (About DOIs).

<http://bit.ly/T0uqzC>

## Reconstructed Face of Extinct "Hobbit" Species Is Startlingly Humanlike

*Anthropologist created the image using forensic techniques for estimating facial appearance from skull form*

By Kate Wong | December 11, 2012

Once upon a time a tiny human species with large feet shared the planet with our own kind. It hunted giant rats and miniature cousins of the elephant, defended its kills from monstrous storks and dodged fearsome dragons.

This is not the plot of a lost Tolkien book. This really happened. I'm referring, of course, to our extinct relative *Homo floresiensis*, which lived on the island of Flores in Indonesia as recently as 17,000 years ago and has for obvious reasons been dubbed the hobbit. It turns out that despite the species' small size, it may have looked rather familiar, according to a scientific reconstruction.

The Flores hobbit is known best from a relatively complete skeleton of an adult female known as LB1 who stood roughly a meter tall and possessed a brain less than a third of the size of our own. Her proportions are completely out of whack with what scientists expected to see in a human species that lived so recently in the grand scheme of things and instead call to mind much earlier human precursors such as Lucy's species, *Australopithecus afarensis*, which lived more than three million years ago. Thus experts have been debating the hobbits' place in the family tree ever since the bones were unveiled in 2004.



*Scientific reconstruction of Homo floresiensis, aka the hobbit. Image: Susan Hayes*

One intriguing theory holds that the hobbits may indicate that human ancestors left Africa far earlier than previously supposed. Conventional wisdom holds that the australopithecines never made it out of the mother land, leaving it to taller, larger-brained *Homo* to colonize the rest of the old world. But maybe, some researchers have suggested, the hobbits were a remnant population of australopithecine that made it out of Africa early on. That would help explain the creature's short stature and small brain, among other primitive features.



Such an explanation makes the new reconstruction of LB1's face all the more surprising to my inexperienced eye. Anthropologist Susan Hayes of the University of Wollongong in Australia created the image using forensic techniques for estimating facial appearance from skull form. It looks a lot like a modern human to me, though I'm sure the tiny size of the head would detract from the resemblance in real life. Hayes revealed the reconstruction on December 10 at the annual Australian Archaeological Conference in Wollongong. An alternate theory holds that the hobbits are dwarfed descendants of *Homo erectus* who evolved their small size as an adaptive response to the limited food resources available on Flores. Such "island dwarfing" has occurred in other species. A third possibility, embraced by a few researchers, is that the tiny bones are simply the remains of diseased modern humans.

[http://www.eurekalert.org/pub\\_releases/2012-12/uoo-aaf121012.php](http://www.eurekalert.org/pub_releases/2012-12/uoo-aaf121012.php)

### **Ancient Australian fossils were on land, not at sea, geologist proposes**

*University of Oregon researcher cites evidence that could shake some limbs on the tree of life*

EUGENE, Ore. - Ancient multicellular fossils long thought to be ancestors of early marine life are remnants of land-dwelling lichen or other microbial colonies, says University of Oregon scientist Gregory Retallack, who has been studying fossil soils of South Australia.

Ediacaran (pronounced EDI-akran) fossils date to 542-635 million years ago. They've been considered fossil jellyfish, worms and sea pens, but are preserved in ways distinct from marine invertebrate fossils. The fossils -- first discovered in 1946 in Australia's Ediacara Hills -- are found in iron-colored impressions similar to plant fossils and microbes in fossil soils.



*Dickinsonia fossils in South Australia, shown here, were likely formed by lichen or other microbial consortia, not from marine invertebrates or giant protists as previously theorized.* Courtesy of Greg Retallack

Retallack, a native of Australia, examined ancient Ediacaran soils with an array of state-of-the-art chemical and microscopic techniques, including an electron microprobe and scanning electron microscope in the UO's CAMCOR Microanalytical Facility headed by John Donovan and rock-analysis technology in the UO's stable isotope laboratory of Ilya Bindeman.

The soils with fossils, Retallack writes in his study, "are distinguished by a surface called 'old elephant skin,' which is best preserved under covering sandstone beds." The healed cracks and lumpy appearance of sandy "old elephant skin" are most like the surface of microbial soil crusts in modern deserts.

"This discovery has implications for the tree of life, because it removes Ediacaran fossils from the ancestry of animals," said Retallack, professor of geological sciences and co-director of paleontological collections at the UO's Museum of Natural and Cultural History. His evidence, mostly gathered from a site in the Flinders Ranges, is presented in a paper placed online ahead of print by the journal *Nature*. "These fossils have been a first-class scientific mystery," he said. "They are the oldest large multicellular fossils. They lived immediately before the Cambrian evolutionary explosion that gave rise to familiar modern groups of animals."

Retallack studied numerous Ediacaran fossils and determined that the diversity reflects a preference by the ancient organisms for "unfrozen, low salinity soils, rich in nutrients, like most terrestrial organisms." Thus the fossils in Australia's iconic red-rock ranges, he concludes, were landlubbers. In his closing paragraph, Retallack outlines implications for a variety of other Ediacaran fossils, that could have been lichens, other microbial consortia, fungal fruiting bodies, slime molds, flanged pedestals of biological soil crusts, and even casts of needle ice.

Ediacaran fossils, he said, represent "an independent evolutionary radiation of life on land that preceded by at least 20 million years the Cambrian evolutionary explosion of animals in the sea." Increased chemical weathering by large organisms on land may have been needed to fuel the demand of nutrient elements by Cambrian animals. Independent discoveries of Cambrian fossils comparable with Ediacaran ones is evidence, he said, that even in the Cambrian, more than 500 million years ago, life on land may have been larger and more complex than life in the sea.

Retallack leaves open the possibility that some Ediacaran fossils found elsewhere in the world may not be land-based in origin, writing in his conclusion that the many different kinds of these fossils need to be tested and re-evaluated. "The key evidence for this new view is that the beds immediately below the cover sandstones in which they are preserved were fossil soils," he said. "In other words the fossils were covered by sand in life position at the top of the soils in which they grew. In addition, frost features and chemical composition of the fossil soils are evidence that they grew in cold dry soils, like lichens in tundra today, rather than in tropical marine lagoons."

Fossil soils are usually recognized from root traces, soil horizons and soil structures, but in rocks of Ediacaran age, before the advent of rooted plants, only the second two criteria can be used to recognize fossil soils. Ediacaran fossil soils, Retallack said, represent ecosystems less effective at weathering than the modern array of ecosystems, so that soil horizons and soil structures are not as well developed as they are in modern soils. "The research conducted by Dr. Retallack helps to unravel the mystery of very ancient life on Earth," said Kimberly Andrews Espy, UO vice president for research and innovation, and dean of the graduate school. "It also serves as an example of how technology, some of it developed at the University of Oregon, can be used to analyze materials from anywhere in the world."

*The American Chemical Society's Petroleum Research Fund supported the fieldwork.*

[http://www.eurekalert.org/pub\\_releases/2012-12/d-sob121112.php](http://www.eurekalert.org/pub_releases/2012-12/d-sob121112.php)

## **Survivors of breast cancer more likely to develop diabetes, and should be screened more closely**

### *Pattern of increased risk related to whether woman received chemotherapy*

A major new study shows that post-menopausal survivors of breast cancer are more likely to develop diabetes than controls without breast cancer. Furthermore, the relationship between breast cancer and diabetes varies depending on whether a breast cancer survivor has undergone chemotherapy. The study is the largest to explore this relationship so far, and is published in *Diabetologia*, the journal of the European Association for the Study of Diabetes (EASD).

An association between diabetes and cancer is becoming increasingly recognised. For instance, women with diabetes have an estimated 20% higher risk of postmenopausal breast cancer. As breast cancer survival rates continue to improve, it is becoming increasingly important to understand the long-term health consequences for survivors as they age. However, to date little research has been carried out on the risk of post-menopausal breast cancer survivors developing diabetes.

In this population-based study, Dr Lorraine Lipscombe (Women's College Hospital, Women's College Research Institute, Toronto, ON, Canada) and colleagues used population-based data from Ontario, Canada to compare the incidence of diabetes among women aged 55 years or older with breast cancer, from 1996 to 2008, with that of age-matched women without breast cancer. They further explored this relationship based on whether the patient had undergone chemotherapy.

They found that, of 24,976 breast cancer survivors and 124,880 controls, 9.7% developed diabetes over a mean follow-up of 5.8 years. The risk of diabetes among breast cancer survivors compared with women without breast cancer began to increase two years after diagnosis, with a 7% increased risk that rose to 21% after 10 years. Among those who received adjuvant chemotherapy (4,404 patients) almost the opposite relationship was found: risk was highest in the first two years after diagnosis (a 24% increased risk compared with controls) and then declined to an 8% increased risk after 10 years.

Dr Lipscombe says: "It is possible that chemotherapy treatment may bring out diabetes earlier in susceptible women. Increased weight gain has been noted in the setting for adjuvant chemotherapy for breast cancer, which may be a factor in the increased risk of diabetes in women receiving treatment. Oestrogen suppression as a result of chemotherapy may also promote diabetes; however this may have been less of a factor in this study where most women were already post-menopausal."

Other factors that may play a part for women with chemotherapy are the glucocorticoid drugs used to treat nausea in chemotherapy, known to cause spikes in blood sugar (acute hyperglycaemia), and the fact that women undergoing chemotherapy could be monitored more closely and thus are more likely to have diabetes detected. A reason that risk decreased in the chemotherapy group over time could be that many of the at-risk women developed diabetes in the first two years, and were thus no longer followed up. In addition, the effects of glucocorticoids are known to wear off over time.

The researchers are unsure why the breast cancer survivors who did not receive chemotherapy saw their risk of diabetes increase compared with control women without cancer. "There is, however, evidence of an association between diabetes and cancer, which may be due to risk factors common to both conditions," says Dr Lipscombe. "One such risk factor is insulin resistance, which predisposes to both diabetes and many types of cancer - initially insulin resistance is associated with high insulin levels and there is evidence that high circulating insulin may increase the risk of cancer. However, diabetes only occurs many years later when insulin levels start to decline - therefore it is possible that cancer risk occurs much earlier than diabetes in insulin-resistant individuals, when insulin levels are high."\*

"These findings support a need for closer monitoring of diabetes among breast cancer survivors," concludes Dr Lipscombe.

[http://www.eurekalert.org/pub\\_releases/2012-12/uoc--evi121212.php](http://www.eurekalert.org/pub_releases/2012-12/uoc--evi121212.php)

## **Emerging virus in raccoons may provide cancer clues**

### ***Brain tumors emerging among raccoons may be linked to a previously unidentified virus***

Rare brain tumors emerging among raccoons in Northern California and Oregon may be linked to a previously unidentified virus discovered by a team of researchers, led by scientists from the University of California, Davis. Their findings, published today in the journal *Emerging Infectious Diseases*, could lead to a better understanding of how viruses can cause cancer in animals and humans.

Necropsies conducted since March 2010 by scientists at the UC Davis School of Veterinary Medicine and UC Davis-led California Animal Health and Food Safety Laboratory found brain tumors in 10 raccoons, nine of which were from Northern California, the article reports. The 10th was sent to UC Davis by researchers at Oregon State University in Corvallis, Ore.

The common factor, found in all of the tumors, was a newly described virus, dubbed raccoon polyomavirus. Researchers suspect this virus contributes to tumor formation.

Polyomaviruses, which are prevalent but rarely cause cancer, do not typically cross from one species to another, so the outbreak is not expected to spread to people or other animals.

Two more raccoons with the tumor and the virus have been found in Yolo and Marin counties since September 2012, when the article was submitted to the journal for publication.

"Raccoons hardly ever get tumors," said study author Patricia Pesavento, a pathologist with the UC Davis School of Veterinary Medicine. "That's why we take notice when we get three tumors, much less 12."

Polyomaviruses are known to cause cancer under laboratory conditions. Less is known about their ability to cause cancer under natural conditions among people, because cancer often takes decades to develop.

Raccoons, with their short lifespans of two to three years, can provide a model for studying how these viruses spread outside the laboratory, how they cause cancer, and how easily they can jump from species to species. Of the 12 raccoons affected, 10 were collected from Marin County. Pesavento said this does not mean the virus is limited to that county, or even to Northern California.

Marin County is home to WildCare, an animal rescue and rehabilitation center that routinely submits animal remains for diagnostic testing, which might result in a sampling bias.

Other California raccoons were submitted by Lindsay Wildlife Museum in Contra Costa County and Sonoma Wildlife Rescue. Pesavento said her lab is collecting specimens and data from other sources across the country, looking for the virus and for raccoon exposure to it.

Pesavento said more research is needed to understand whether an environmental toxin, genetics or other explanation is contributing to the cancer. The study said that raccoons are exposed daily to human waste, garbage, environmental toxins and environmental pathogens as they travel along sewer and water lines.

"This is just the beginning of a story," said Pesavento, adding that high rates of cancer among wildlife are found in animals that live in close proximity to humans. "Wildlife live in our fields, our trash cans, our sewer lines, and that's where we dump things. Humans need to be guardians of the wildlife-human interface, and raccoons are important sentinel animals. They really are exquisitely exposed to our waste. We may be contributing to their susceptibility in ways we haven't discovered."

Infectious pathogens, such as viruses, are associated with 15-20 percent of all human cancers worldwide, according to the American Cancer Society. For example, human papillomavirus can lead to cervical cancer. Feline leukemia virus, for which UC Davis developed a vaccine, can cause cancer in cats.

UC Davis also continues to study Marek's disease, a deadly virus in chickens that is providing insight into human cancer.

"This work to investigate natural associations of cancer verifies the importance of our One Health approach to addressing complex biomedical problems, such as viral causes of cancer," said Michael Lairmore, dean of the School of Veterinary Medicine, of which the UC Davis One Health Institute is a part.

"Understanding how infectious agents may contribute to cancer in animals has provided fundamental new knowledge on the cause of cancer in people."

*The study was funded through The Bernice Barbour Foundation, the UC Davis Center for Companion Animal Health, and Meadowview Foundation.*

*The study's authors include lead author Florante Dela Cruz, Federico Giannitti and Leslie Woods from UC Davis; Eric Delwart from University of California, San Francisco, and Blood Systems Research Institute in San Francisco; Linlin Li from Blood Systems Research Institute; and Luis Del Valle from Louisiana State University in New Orleans.*



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## Caltech-led astronomers discover galaxies near cosmic dawn

*Researchers conduct first census of the most primitive and distant galaxies seen*

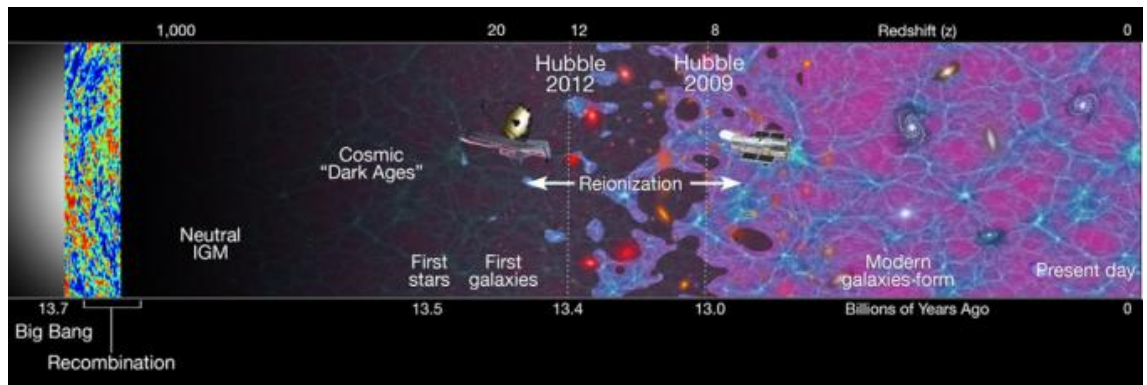
Written by Marcus Woo

PASADENA, Calif. - A team of astronomers led by the California Institute of Technology (Caltech) has used NASA's Hubble Space Telescope to discover seven of the most primitive and distant galaxies ever seen. One of the galaxies, the astronomers say, might be the all-time record holder - the galaxy as observed existed when the universe was merely 380 million years old. All of the newly discovered galaxies formed more than 13 billion years ago, when the universe was just about 4 percent of its present age, a period astronomers call the "cosmic dawn," when the first galaxies were born. The universe is now 13.7 billion years old. The new observations span a period between 350 million and 600 million years after the Big Bang and represent the first reliable census of galaxies at such an early time in cosmic history, the team says. The astronomers found that the number of galaxies steadily increased as time went on, supporting the idea that the first galaxies didn't form in a sudden burst but gradually assembled their stars. Because it takes light billions of years to travel such vast distances, astronomical images show how the universe looked during the period, billions of years ago, when that light first embarked on its journey. The farther away astronomers peer into space, the further back in time they are looking. In the new study, which was recently accepted for publication in the *Astrophysical Journal Letters*, the team has explored the deepest reaches of the cosmos - and therefore the most distant past - that has ever been studied with Hubble.

"We've made the longest exposure that Hubble has ever taken, capturing some of the faintest and most distant galaxies," says Richard Ellis, the Steele Family Professor of Astronomy at Caltech and the first author of the paper. "The added depth and our carefully designed observing strategy have been the key features of our campaign to reliably probe this early period of cosmic history." The results are the first from a new Hubble survey that focused on a small patch of sky known as the Hubble Ultra Deep Field (HUDF), which was first studied nine years ago. The astronomers used Hubble's Wide Field Camera 3 (WFC3) to observe the HUDF in near-infrared light over a period of six weeks during August and September 2012.

To determine the distances to these galaxies, the team measured their colors using four filters that allow Hubble to capture near-infrared light at specific wavelengths. "We employed a filter that has not been used in deep imaging before, and undertook much deeper exposures in some filters than in earlier work, in order to convincingly reject the possibility that some of our galaxies might be foreground objects," says team member James Dunlop of the Institute for Astronomy at the University of Edinburgh. The carefully chosen filters allowed the astronomers to measure the light that was absorbed by neutral hydrogen, which filled the universe beginning about 400,000 years after the Big Bang. Stars and galaxies started to form roughly 200 million years after the Big Bang. As they did, they bathed the cosmos with ultraviolet light, which ionized the neutral hydrogen by stripping an electron from each hydrogen atom. This so-called "epoch of reionization" lasted until the universe was about a billion years old. If everything in the universe were stationary, astronomers would see that only a specific wavelength of light was absorbed by neutral hydrogen. But the universe is

expanding, and this stretches the wavelengths of light coming from galaxies. The amount that the light is stretched - called the redshift - depends on distance: the farther away a galaxy is, the greater the redshift.



*This timeline shows the evolution of the universe since the Big Bang. The new observations, labeled "Hubble 2012," explored the deepest reaches of the cosmos that has ever been studied with Hubble, going back about 13.4 billion years -- around when the first galaxies were being formed. Previously, the universe was in the so-called Dark Ages, before there were any stars to light up the cosmos. During reionization, ultraviolet light from the newly formed stars and galaxies ionized the neutral hydrogen that permeated the universe. The dashed line labeled Hubble 2009 represents the last set of observations of HUDF. NASA/ESA*

As a result of this cosmic expansion, astronomers observe that the absorption of light by neutral hydrogen occurs at longer wavelengths for more distant galaxies. The filters enabled the researchers to determine at which wavelength the light was absorbed; this revealed the distance to the galaxy - and therefore the period in cosmic history when it is being formed. Using this technique to penetrate further and further back in time, the team found a steadily decreasing number of galaxies.

"Our data confirms that reionization is a drawn-out process occurring over several hundred million years with galaxies slowly building up their stars and chemical elements," says coauthor Brant Robertson of the University of Arizona in Tucson. "There wasn't a single dramatic moment when galaxies formed; it's a gradual process." The new observations - which pushed Hubble to its technical limits - hint at what is to come with next-generation infrared space telescopes, the researchers say. To probe even further back in time to see ever more primitive galaxies, astronomers will need to observe in wavelengths longer than those that can be detected by Hubble. That's because cosmic expansion has stretched the light from the most distant galaxies so much that they glow predominantly in the infrared. The upcoming James Webb Space Telescope, slated for launch in a few years, will target those galaxies. "Although we may have reached back as far as Hubble will see, Hubble has, in a sense, set the stage for Webb," says team member Anton Koekemoer of the Space Telescope Science Institute in Baltimore. "Our work indicates there is a rich field of even earlier galaxies that Webb will be able to study."

*The title of the Astrophysical Journal Letters paper is, "The Abundance of Star-Forming Galaxies in the Redshift Range 8.5 to 12: New Results from the 2012 Hubble Ultra Deep Field Campaign." In addition to Ellis, Dunlop, Robertson, and Koekemoer, the other authors on the Astrophysical Journal Letters paper are Matthew Schenker of Caltech; Ross McLure, Rebecca Bowler, Alexander Rogers, Emma Curtis-Lake, and Michele Cirasuolo of the Institute for Astronomy at the University of Edinburgh; Yoshiaki Ono and Masami Ouchi of the University of Tokyo; Evan Schneider of the University of Arizona; Daniel Stark of the University of Cambridge; Stéphane Charlot of the Institut d'Astrophysique de Paris; and Steven Furlanetto of UCLA. The research was supported by the Space Telescope Science Institute, the European Research Council, the Royal Society, and the Leverhulme Trust.*

<http://www.sciencedaily.com/releases/2012/12/121212092102.htm>

## **Opiates Already in Body May Encourage Cancer Growth, Certain Medications Could Slow It**

### ***Opioids already in the body can enhance the malignant tendencies of human cancer cells***

A study led by University of Chicago researcher Patrick A. Singleton, Ph.D. and published in the journal *Anesthesiology* has shown that, even without the addition of further opioids such as morphine, opioids already in the body can enhance the malignant tendencies of human cancer cells.

Dr. Singleton's study adds support to mounting evidence that the mu opioid receptor in cancer cells influences cancer progression and spread, and could become a therapeutic target for cancer treatment.

"If confirmed clinically, this could influence how we do surgical anesthesia for our cancer patients," said Dr. Singleton, who is Assistant Professor of Medicine at the University of Chicago Medical Center. "There is epidemiological evidence to suggest that the type of anesthesia used during cancer surgery may influence tumor recurrence."

In their study, Dr. Singleton and his research team, including Jonathan Moss, M.D., Ph.D., injected human lung cancer cells with additional copies of the mu opioid receptor into mice based on their prior observations that cells from certain types of human lung cancer had five to 10 times as many opioid receptors as normal cells. Tumors in the mice injected with the cancer cells having the additional copies of the mu opioid receptor grew more than twice as fast as those injected with cells that lacked the extra receptors, and were 20 times more likely to spread to other parts of the body.

Dr. Moss, who has researched the effects of opioids on cancer extensively, suggests that these results support the growing focus of a potential therapeutic role for drugs known as opioid antagonists, one of which is called methylnaltrexone (MNTX). MNTX is approved to treat opioid-induced constipation without disrupting pain relief in palliative care patients. According to Dr. Moss, Professor of Anesthesiology and Critical Care at the University of Chicago Medical Center, the beneficial effects could be far greater: "In compassionate-use studies prior to its approval, we noted that some cancer patients receiving MNTX to treat opioid-induced constipation lived longer than expected," said Dr. Moss. "These were patients with advanced cancer and a life expectancy of one of two months, yet several lived another five or six months. This led us to question whether these patients were living longer because of better gut function or whether there was something about blocking the mu opioid receptor that influenced tumor progression."

In a series of laboratory studies, Drs. Singleton and Moss found that drugs which blocked mu opioid receptors reduced cancer growth in animals and helped prevent further invasion and spread of cancer cells. Further,

tumors did not grow in mice that lacked the mu opioid receptor. Despite the growing body of laboratory evidence suggesting that the mu opioid receptor plays a role in tumor progression, Drs. Singleton and Moss cautioned that no clinical trials exist that demonstrate a direct effect of the receptor blockade on cancer growth or treatment.

*Frances E. Lennon, Tamara Mirzapoiazova, Bolot Mambetsariev, Ravi Salgia, Jonathan Moss, Patrick A. Singleton. Overexpression of the  $\mu$ -Opioid Receptor in Human Non-Small Cell Lung Cancer Promotes Akt and mTOR Activation, Tumor Growth, and Metastasis. Anesthesiology, 2012; 116 (4): 857 DOI: 10.1097/ALN.0b013e31824babe2*

<http://www.sciencedaily.com/releases/2012/12/121212130709.htm>

## **Was Life Inevitable? New Paper Pieces Together Metabolism's Beginnings**

*Describing how living organisms emerged from Earth's abiotic chemistry has remained a conundrum for scientists*

Describing how living organisms emerged from Earth's abiotic chemistry has remained a conundrum for scientists, in part because any credible explanation for such a complex process must draw from fields spanning the reaches of science.

A new synthesis by two Santa Fe Institute researchers offers a coherent picture of how metabolism, and thus all life, arose. The study, published December 12, 2012, in the journal *Physical Biology*, offers new insights into how the complex chemistry of metabolism cobbled itself together, the likelihood of life emerging and evolving as it did on Earth, and the chances of finding life elsewhere.

"We're trying to bring knowledge across disciplines into a unified whole that fits the essentials of metabolism development," says co-author Eric Smith, a Santa Fe Institute External Professor.

Creating life from scratch requires two abilities: fixing carbon and making more of yourself. The first, essentially hitching carbon atoms together to make living matter, is a remarkably difficult feat. Carbon dioxide (CO<sub>2</sub>), of which Earth has plenty, is a stable molecule; the bonds are tough to break, and a chemical system can only turn carbon into biologically useful compounds by way of some wildly unstable in-between stages.

As hard as it is to do, fixing carbon is necessary for life. A carbon molecule's ability to bond stably with up to four atoms makes it phenomenally versatile, and its abundance makes it suitable as a backbone for trillions of compounds. Once an organized chemical system can harness and manipulate carbon, it can expand and innovate in countless ways.

In other words, carbon fixation is the centerpiece of metabolism -- the basic process by which cells take in chemicals from their environments and build them into products they need to live. It's also the link between the geochemistry of Earth and the biochemistry of life.

In a paper earlier this year, Smith and Santa Fe Institute Omidyar Fellow Rogier Braakman mapped the most primitive forms of carbon fixation onto major, early branching points in the tree of life (*PLoS Computational Biology*, April 18, 2012). Now, the two researchers have drawn from geochemistry, biochemistry, evolution, and ecology to detail the likeliest means by which molecules lurched their way from rocks to cells.

Their 62-page "Logic of Metabolism" paper presents a new, coherent picture of how this complex system fits together.

What started as wonky geochemical mechanisms were sequentially replaced and fortified by biological ones, the authors believe. "Think of life like an onion emerging in layers, where each layer functions as a feedback mechanism that stabilizes and improves the ability to fix carbon," says Braakman.

Carbon fixing and other chemical sub-processes that together constitute metabolism each comprise dozens of steps; some are quick and easy turnkey reactions with simple molecules, others require highly specific chemical helpers, or catalysts.

The parts of metabolism that guide carbon fixation through its unstable intermediate stages fall into the latter category, requiring help. But these seemingly unlikely reactions are remarkably consistent across all living systems. In fact, says Braakman, their ubiquity and the difficulty with which they are forged make them the chemical constraints within which all living systems operate -- in a sense, the scaffolding for the tree of life. It's these dependable regularities of hierarchy and modularity, amid the panoply of reactions comprising metabolism, that stabilize the system and enable its complexity.

Braakman and Smith describe specific features of metabolism and sub-divide helper metabolites by their functions. For example, vitamin B<sub>9</sub>, a complex molecule in the 'cofactor' class, facilitates the (otherwise unstable) incorporation of one-carbon compounds into metabolism.

In mapping the chemical pathways to life's emergence, the researchers touch on a more existential question: How likely was it for life to have developed at all? Extraordinarily so, says Braakman. "Metabolism appears to be an 'attractor state' within organic chemistry, where it was likely to be selected regardless of earlier stages of chemical evolution" in the chaotic, high-energy conditions of prebiotic Earth, he says.



Can it happen elsewhere? Possibly, even probably, he says. Rocky planets usually have cores chemically similar to ours, so if a planet is volcanically (and perhaps tectonically) active and has an ocean, it will probably have hydrothermal vents that spew chemicals, creating the potential conditions for life, Braakman says. In fact, the physics of star and planet formation make the chances of such conditions pretty reasonable.

Smith cautions, however, that we still have much to learn about the chemical and physical conditions that might lead to life-like organization, but he hopes their paper will at least "lead to experimental questions that focus more directly on the key functions that link metabolism to geochemistry."

Rogier Braakman, Eric Smith. *The compositional and evolutionary logic of metabolism*. *Physical Biology*, 2013; 10 (1): 011001 DOI: 10.1088/1478-3975/10/1/011001

Rogier Braakman, Eric Smith. *The Emergence and Early Evolution of Biological Carbon-Fixation*. *PLoS Computational Biology*, 2012; 8 (4): e1002455 DOI: 10.1371/journal.pcbi.1002455

<http://www.sciencedaily.com/releases/2012/12/121212205736.htm>

## **Depression Eased Quickly With Experimental Drug**

### ***Works in Brain Like Ketamine, With Fewer Side Effects, Study Suggests***

A drug that works through the same brain mechanism as the fast-acting antidepressant ketamine briefly improved treatment-resistant patients' depression symptoms in minutes, with minimal untoward side effects, in a clinical trial conducted by the National Institutes of Health. The experimental agent, called AZD6765, acts through the brain's glutamate chemical messenger system.

Existing antidepressants available through prescription, which work through the brain's serotonin system, take a few weeks to work, imperiling severely depressed patients, who can be at high risk for suicide. Ketamine also works in hours, but its usefulness is limited by its potential for dissociative side-effects, including hallucinations. It is being studied mostly for clues to how it works.

"Our findings serve as a proof of concept that we can tap into an important component of the glutamate pathway to develop a new generation of safe, rapid-acting practical treatments for depression," said Carlos Zarate, M.D., of the NIH's National Institute of Mental Health, which conducted the research.

Zarate, and colleagues, reported on their results online Dec. 1, 2012 in the journal *Biological Psychiatry*.

AZD6765, like ketamine, works by blocking glutamate binding to a protein on the surface of neurons, called the NMDA receptor. It is a less powerful blocker of the NMDA receptor, which may be a reason why it is better tolerated than ketamine.

About 32 percent of 22 treatment-resistant depressed patients infused with ASD6765 showed a clinically meaningful antidepressant response at 80 minutes after infusion that lasted for about half an hour -- with residual antidepressant effects lasting two days for some. By contrast, 52 percent of patients receiving ketamine show a comparable response, with effects still detectable at seven days. So a single infusion of ketamine produces more robust and sustained improvement, but most patients continue to experience some symptoms with both drugs.

However, depression rating scores were significantly better among patients who received AZD6765 than in those who received placebos. The researchers deemed this noteworthy, since, on average, these patients had failed to improve in seven past antidepressant trials, and nearly half failed to respond to electroconvulsive therapy (ECT). The patients reported only minor side effects, such as dizziness and nausea, which were not significantly different from those experienced with the placebo.

Zarate and colleagues say their results warrant further trials with AZD6765, testing whether repeated infusions a few times per week or higher doses might produce longer-lasting results.

Carlos A. Zarate, Daniel Mathews, Lobna Ibrahim, Jose Franco Chaves, Craig Marquardt, Immaculata Ukoh, Libby Jolkovsky, Nancy E. Brutsche, Mark A. Smith, David A. Luckenbaugh. *A Randomized Trial of a Low-Trapping Nonselective N-Methyl-D-Aspartate Channel Blocker in Major Depression*. *Biological Psychiatry*, 2012; DOI: 10.1016/j.biopsych.2012.10.019

<http://www.sciencedaily.com/releases/2012/12/121212205720.htm>

## **Brain Damage Triggered by Mini-Stroke Detailed**

### ***Study details how "mini-strokes" cause prolonged periods of brain damage, resulting in cognitive impairment***

A new study appearing December 12 in the *Journal of Neuroscience* details for the first time how "mini-strokes" cause prolonged periods of brain damage and result in cognitive impairment. These strokes, which are often imperceptible, are common in older adults and are believed to contribute to dementia.

"Our research indicates that neurons are being lost as a result of delayed processes following a mini-stroke that may differ fundamentally from those of acute ischemic events," said Maiken Nedergaard, M.D., D.M.Sc., the lead author of the study and professor of Neurosurgery at the University of Rochester Medical Center (URMC).

"This observation suggests that the therapeutic window to protect cells after these tiny strokes may extend to days and weeks after the initial injury."

The prevalence of mini-strokes, or microinfarcts, has only been recently appreciated because common imaging techniques, such as MRI, are typically not sensitive enough to detect these microscopic injuries.

Similar to severe ischemic strokes, mini-strokes are caused when blood flow is blocked to a small area of the brain, usually by particle that travelled there from another part of the body. But unlike acute ischemic strokes -- which bring about immediate symptoms such as numbness, blurry vision, and slurred speech -- mini-strokes usually pass without notice. However, it is increasingly appreciated that these smaller strokes have a lasting impact on neurological function.

Microinfarcts are far more common than previously understood; it is believed that about 50 percent of individuals over the age of 60 have experienced at least one mini-stroke. Studies have also correlated the presence of mini-strokes with the symptoms of dementia. An estimated 55 percent of individuals with mild dementia and upwards of 70 percent of individuals with more severe symptoms show evidence of past mini-strokes. This association has led researchers to believe that these mini-strokes may be key contributors to age-related cognitive decline and dementia.

Nedergaard and her colleagues were the first to develop an animal model in which the complex progression and, ultimately, the cognitive impact of mini-strokes could be observed. Her team found that, in most instances, these strokes result in a prolonged period of damage to the brain.

A small fraction of these microinfarcts unfold in a manner similar to acute strokes; cell death is immediate and the brain quickly seals off the site of the stroke and begins to "digest" the damaged tissue. However, the researchers also identified a second and far more common form of mini-stroke -- which they labeled incomplete lesions -- where the cell death can drag on for several weeks.

"In most microinfarcts the injury is incomplete," said Nedergaard. "There is no scar tissue to separate the stroke site from the rest of the brain and the cells that would normally support the neurons may not function properly. As a result, the neurons at the site continue to slowly die like a smoldering fire. This suggests that, unlike acute ischemic strokes where the cell death occurs in the first 24 hours, there is a longer period in which we can medically intervene and stop the neuronal death that results from mini-strokes."

The researchers then attempted to determine the cognitive impact of microinfarcts. Mice who were victims of mini-strokes underwent a series of experiments during which they had to recall objects or respond to certain audio cues. The researchers observed that the mice with mini-strokes were far more likely to fail these tasks -- suggesting neurological impairment -- compared to healthy mice.

Additional co-authors include Jeffrey Iliff, Yonghong Liao, Michael Chen, Matthew Shinseki, Arun Venkataraman, and Jessica Cheung with the Center for Translational Neuromedicine at UPMC and Minghuan Wang, Wei Wang with the Huazhong University of Science and Technology in China. The study was supported with funding from the National Institutes of Health, the U.S. Department of Defense, and the Harold and Leila Y. Mathers Charitable Foundation.

M. Wang, J. J. Iliff, Y. Liao, M. J. Chen, M. S. Shinseki, A. Venkataraman, J. Cheung, W. Wang, M. Nedergaard. *Cognitive Deficits and Delayed Neuronal Loss in a Mouse Model of Multiple Microinfarcts*. *Journal of Neuroscience*, 2012; 32 (50): 17948 DOI: 10.1523/JNEUROSCI.1860-12.2012

[http://www.eurekalert.org/pub\\_releases/2012-12/ul-yct121312.php](http://www.eurekalert.org/pub_releases/2012-12/ul-yct121312.php)

## **Your Christmas tree and its genome have remained very much the same over the last 100 million years**

***Study reveals that the genome of conifers has remained almost unchanged for over 100 million years***

Quebec City - A study published by Université Laval researchers and their colleagues from the Canadian Forest Service reveals that the genome of conifers such as spruce, pine, and fir has remained very much the same for over 100 million years. This remarkable genomic stability explains the resemblance between today's conifers and fossils dating back to the days when dinosaurs roamed the Earth. Details of this finding are presented in a recent issue of the journal BMC Biology.

The team supervised by Professor Jean Bousquet, who holds the Canada Research Chair in Forest and Environmental Genomics, came to this conclusion after analyzing the genome of conifers and comparing it to that of flowering plants. Both plant groups stem from the same ancestor but diverged some 300 million years ago.

Researchers compared the genome macrostructure for 157 gene families present both in conifers and flowering plants. They observed that the genome of conifers has remained particularly stable for at least 100 million years, while that of flowering plants has undergone major changes in the same period. "That doesn't mean there haven't been smaller scale modifications such as genetic mutations," points out Jean Bousquet. "However, the

macrostructure of the conifer genome has been remarkably stable over the ages," adds the professor from the Université Laval Faculty of Forestry, Geography, and Geomatics.

This great stability goes hand in hand with the low speciation rate of conifers. The world is currently home to only 600 species of conifers, while there are over 400,000 species of flowering plants. "Conifers appear to have achieved a balance with their environment very early," remarks Professor Bousquet. "Still today, without artifice, these plants thrive over much of the globe, particularly in cold climates. In contrast, flowering plants are under intense evolutionary pressure as they battle for survival and reproduction," he concludes.

*In addition to Bousquet, the study's coauthors are Nathalie Pavy, Betty Pelgas, Jérôme Laroche, Philippe Rigault, and Nathalie Isabel. This project was made possible thanks to the financial support of Genome Canada, Génome Québec, Natural Resources Canada, and the Natural Sciences and Engineering Research Council of Canada.*

[http://www.eurekalert.org/pub\\_releases/2012-12/uoo-oss121312.php](http://www.eurekalert.org/pub_releases/2012-12/uoo-oss121312.php)

## **OU study suggests the bacterial ecology that lives on humans has changed in the last 100 years**

### ***Insights from 'Characterizing Extinct Human Gut Microbiomes'***

A University of Oklahoma-led study has demonstrated that ancient DNA can be used to understand ancient human microbiomes. The microbiomes from ancient people have broad reaching implications for understanding recent changes to human health, such as what good bacteria might have been lost as a result of our current abundant use of antibiotics and aseptic practices.

Cecil M. Lewis Jr., professor of anthropology in the OU College of Arts and Sciences and director of the OU Molecular Anthropology Laboratory, and Raul Tito, OU Research Associate, led the research study that analyzed microbiome data from ancient human fecal samples collected from three different archaeological sites in the Americas, each dating to over 1000 years ago.

In addition, the team provided a new analysis of published data from two samples that reflect rare and extraordinary preservation: Otzi the Iceman and a soldier frozen for 93 years on a glacier.

"The results support the hypothesis that ancient human gut microbiomes are more similar to those of non-human primates and rural non-western communities than to those of people living a modern lifestyle in the United States," says Lewis.

"From these data, the team concluded that the last 100 years has been a time of major change to the human gut microbiome in cosmopolitan areas."

"Dietary changes, as well as the widespread adoption of various aseptic and antibiotic practices have largely benefited modern humans, but many studies suggest there has been a cost, such as a recent increase in autoimmune related risks and other health states," states Lewis.

"We wish to reveal how this co-evolutionary relationship between humans and bacteria has changed, while providing the foundation for interventions to reconstruct what has been lost. One way to do this is to study remote communities and non-human primates. An alternative path is to look at ancient samples and see what they tell us," Lewis says.

"An argument can be made that remote traditional communities are not truly removed from modern human ecologies. They may receive milk or other food sources from the government, which could alter the microbial ecology of the community.

Our evolutionary cousins, non-human primates are important to consider. However, the human-chimp common ancestor was over six million years ago, which is a lot of time for microbiomes to evolve distinct, human signatures."

Retrieving ancient human microbiome data is complementary to these studies. However, studying ancient microbiomes is not without problems. Assuming DNA preserves, there is also a problem with contamination and modification of ancient samples, both from the soil deposition, and from other sources, including the laboratory itself.

"In addition to laboratory controls in our study, we use an exciting new quantitative approach called source tracking developed by Dan Knights from Rob Knight's Laboratory at the University of Colorado in Boulder, which can estimate how much of the ancient microbiome data is consistent with the human gut, rather than other sources, such as soil," explains Lewis.

"We discovered that certain samples have excellent gut microbiome signatures, opening the door for deeper analyses of the ancient human gut, including a better understanding of the ancient humans themselves, such as learning more about their disease burdens, but also learning more about what has changed in our gut today."

*The paper, "Insights from Characterizing Extinct Human Gut Microbiomes," will be published in the journal PLOS ONE.*



[http://www.eurekalert.org/pub\\_releases/2012-12/yu-dhc121312.php](http://www.eurekalert.org/pub_releases/2012-12/yu-dhc121312.php)

**Despite hype, costly prostate cancer treatment offers little relief from side effects**  
*Prostate cancer patients receiving proton radiotherapy experienced minimal relief from side effects compared to patients undergoing intensity modulated radiotherapy*

Prostate cancer patients receiving the costly treatment known as proton radiotherapy experienced minimal relief from side effects such as incontinence and erectile dysfunction, compared to patients undergoing a standard radiation treatment called intensity modulated radiotherapy (IMRT), Yale School of Medicine researchers report in the Journal of the National Cancer Institute.

Standard treatments for men with prostate cancer, such as radical prostatectomy and IMRT, are known for causing adverse side effects such as incontinence and erectile dysfunction. Proponents of proton radiotherapy argue that the physical properties of protons may decrease these common side effects.

"Proton radiotherapy is increasing in popularity and more and more proton centers are being built throughout the country," said the study's lead author James Yu, M.D., assistant professor of therapeutic radiology at Yale Cancer Center and member of the Yale Cancer Outcomes, Public Policy, and Effectiveness Research (COPPER) Center at Yale. "However, there is a surprising lack of information about whether proton radiotherapy is actually superior to IMRT."

To find out, the Yale COPPER team studied a national sample of about 30,000 men with Medicare coverage who received treatment with either IMRT or proton radiotherapy for prostate cancer from 2008 to 2009. During this time, there were six centers offering proton radiotherapy in the United States and the authors found that some men travelled across the country for the treatment.

The team found that the incidence of complications such as problems with urinary function was slightly lower for proton radiotherapy at six months after treatment, but by 12 months after treatment there was no longer any difference. Despite the fact that there was no longer term benefit to the treatment in terms of side effects, Medicare paid over \$32,000 per course of treatment, compared to less than \$19,000 for a course of IMRT.

"We were surprised by these findings," said Cary Gross, senior author of the study and co-director of the COPPER Center. "Cancer centers are paying up to \$100 million to build their own proton centers, and patients are travelling long distances to undergo proton therapy because the conventional wisdom has been that proton radiotherapy is better than IMRT. Our results suggest that this enthusiasm for proton therapy may be premature; it remains to be seen how proton radiotherapy will compare to IMRT at 10 or 15 years post-treatment."

*Other authors on the study include Pamela Soulos, Jeph Herrin, Laura Cramer, Arnold Potosky, and Kenneth Roberts.*

*The study was funded by a grant from the National Cancer Institute (R01CA149045). Yu is also supported by the National Center for Research Resources (NCRR) and the National Center for Advancing Translational Science (NCATS), components of the National Institutes of Health (NIH), and NIH roadmap for medical research (KL2 RR024138).*

*Citation: JNCI: 10.1093/jnci/djs463*

[http://www.eurekalert.org/pub\\_releases/2012-12/msu-abc121312.php](http://www.eurekalert.org/pub_releases/2012-12/msu-abc121312.php)

**Countering brain chemical could prevent suicides**

*First proof that glutamate is linked to suicidal behavior*

EAST LANSING, Mich. - Researchers have found the first proof that a chemical in the brain called glutamate is linked to suicidal behavior, offering new hope for efforts to prevent people from taking their own lives.

Writing in the journal Neuropsychopharmacology, Michigan State University's Lena Brundin and an international team of co-investigators present the first evidence that glutamate is more active in the brains of people who attempt suicide. Glutamate is an amino acid that sends signals between nerve cells and has long been a suspect in the search for chemical causes of depression.

"The findings are important because they show a mechanism of disease in patients," said Brundin, an associate professor of experimental psychiatry in MSU's College of Human Medicine. "There's been a lot of focus on another neurotransmitter called serotonin for about 40 years now. The conclusion from our paper is that we need to turn some of that focus to glutamate."

Brundin and colleagues examined glutamate activity by measuring quinolinic acid -- which flips a chemical switch that makes glutamate send more signals to nearby cells -- in the spinal fluid of 100 patients in Sweden. About two-thirds of the participants were admitted to a hospital after attempting suicide and the rest were healthy.

They found that suicide attempters had more than twice as much quinolinic acid in their spinal fluid as the healthy people, which indicated increased glutamate signaling between nerve cells. Those who reported the strongest desire to kill themselves also had the highest levels of the acid.

The results also showed decreased quinolinic acid levels among a subset of patients who came back six months later, when their suicidal behavior had ended.

The findings explain why earlier research has pointed to inflammation in the brain as a risk factor for suicide.

The body produces quinolinic acid as part of the immune response that creates inflammation.

Brundin said anti-glutamate drugs are still in development, but could soon offer a promising tool for preventing suicide. In fact, recent clinical studies have shown the anesthetic ketamine - which inhibits glutamate signaling - to be extremely effective in fighting depression, though its side effects prevent it from being used widely today.

In the meantime, Brundin said physicians should be aware of inflammation as a likely trigger for suicidal behavior. She is partnering with doctors in Grand Rapids, Mich., to design clinical trials using anti-inflammatory drugs. "In the future, it's likely that blood samples from suicidal and depressive patients will be screened for inflammation," Brundin said. "It is important that primary health care physicians and psychiatrists work closely together on this."

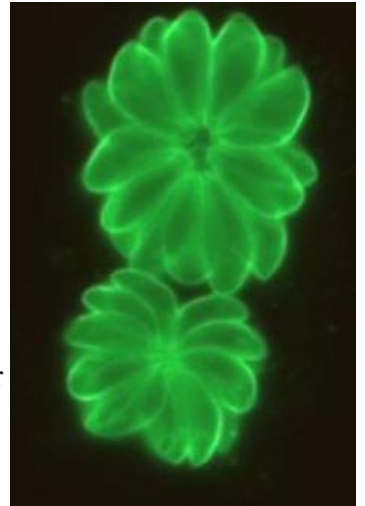
[http://www.eurekalert.org/pub\\_releases/2012-12/cp-nsb120612.php](http://www.eurekalert.org/pub_releases/2012-12/cp-nsb120612.php)

### **New study brings long-sought vaccines for deadly parasite closer to reality**

*The findings could lead to the development of long-sought vaccines to protect against *Toxoplasma gondii**

One major cause of illness from food-borne diseases is the parasite *Toxoplasma gondii* (*T. gondii*). New insights into how the immune system combats *T. gondii* are provided in a study published by Cell Press December 13th in the journal *Immunity*. The findings could lead to the development of long-sought vaccines to protect against *T. gondii* and related parasites.

To fight off pathogens, the immune system relies on Toll-like receptors (TLRs)—a class of proteins that recognize microbes and activate immune responses. The important role of TLR11 in recognizing the *T. gondii* infection was previously demonstrated by a team led by Sankar Ghosh of Columbia University and Alan Sher of the National Institute of Allergy and Infectious Diseases. But scientists had not yet identified any TLRs—including TLR11—that could promote survival in infected animals.



*This is an image of *T. gondii*. Sankar Ghosh*

In the new study, Ghosh, Sher, and their collaborators focused on the previously uncharacterized TLR12 because it is closely related to TLR11 and physically interacts with that receptor, suggesting that the two might work together to mount immune responses. When they genetically engineered mice to lack TLR12, they found that immune cells could not recognize or protect against *T. gondii*, and these mice quickly succumbed to infection. Although both TLR11 and TLR12 activate overlapping immune responses to *T. gondii* in certain types of cells, TLR12 also triggers responses in a distinct set of immune cells to promote survival.

"Prior to this study, TLR12 had no known function in the immune system, and it was not known what pathogen this receptor recognized," Ghosh says. "We have demonstrated that TLR12 is essential for resistance to *T. gondii* in mice."

Because TLR12 also recognized another related parasite, the findings could have broad clinical implications.

"By investigating how immune cells expressing TLR12 organize the immune response against *T. gondii* infection, we hope to identify new means of promoting protective immune responses against *T. gondii* and potentially other important parasite pathogens," Ghosh says.

*Koblansky et al.: "Recognition of profilin by toll-like receptor 12 is critical for host resistance to *Toxoplasma gondii*."*

[http://www.eurekalert.org/pub\\_releases/2012-12/v-c121312.php](http://www.eurekalert.org/pub_releases/2012-12/v-c121312.php)

### **Common anesthetic agents can be harmful for the development of the fetus**

*Anesthetic typically used during surgery on pregnant mothers may have a negatively effect fetal development*

An anesthetic regimen typically used during surgery on pregnant mothers appears to have a negative effect on the development of the fetus, according to a new study on mice conducted by neurobiologists from the National Center for Toxicological Research, in Arizona.

In the article 'Inhalation Anesthesia-Induced Neuronal Damage and Gene Expression Changes in Developing Rat Brain' published earlier this month in *Systems Pharmacology*, an open access journal by Versita – Dr. Fang Liu and Dr. Cheng Wang describe the effect of major, commonly used anesthetic compounds – Nitrous Oxide (N<sub>2</sub>O), N-methyl-D-aspartate (NMDA) receptor antagonist, and isoflurane (ISO) on the developing brain of post-natal rats. Looking into the mechanisms through which N<sub>2</sub>O + ISO cause neurotoxicity in the developing brain, the authors suggest multiple factors are involved in neuronal cell death inducing effects (cascades) of N<sub>2</sub>O + ISO.

As with any medical intervention performed during pregnancy, expectant mothers are concerned about the possibility of undergoing surgery or other medical procedures that require anesthesia and may be harmful to both the woman and her baby. Understandably, there is concern for the development of the fetus, but also for the immediate health of the mother and possible preterm labor. Until recently most studies of documented use have admittedly shown that inhaled anesthetics pose no risks for pregnant women.

Contrary to previous research findings, it has now emerged that the combination of N<sub>2</sub>O + ISO can change the gene expression of brain tissues and may be related to the elevated neuronal cell death as indicated by an increased number of apoptotic cells in frontal cortical levels compared with the control. The researchers came to this novel conclusion owing to the use of microarray data and cell analysis. They demonstrated that the combination of N<sub>2</sub>O + ISO induces a significant change in gene expression and cell death of neuronal tissues in post-natal rats. The brain tissue of post-natal rats seems to be more sensitive to N<sub>2</sub>O + ISO when compared to adult brains tissues.

Considering that pregnant women and neonates are subjected to anesthesia with N<sub>2</sub>O + ISO in determined clinical procedures, it could potentially affect the brain tissues of fetuses or neonates in long-term exposure to N<sub>2</sub>O + ISO.

"The findings come as a major step forward in better understanding of this phenomenon", says Prof. Diego Bonatto from the Department of Molecular Biology and Biotechnology at the Federal University of Rio Grande do Sul. A study in new-born rats published in 2003 indicated that exposure to various anesthetic agents caused neurodegeneration in the developing rat brain. In 2005 however, a more recent study on sheep carried out by researchers from Duke University Medical Center revealed that the moderate exposure to inhalation anesthetic during pregnancy is not harmful to the fetus.

This research deserves attention: for the first time the authors managed to show that the administration of N<sub>2</sub>O + ISO to neonates or pregnant women can potentially induce changes in molecular mechanisms associated to the cell survival, especially in brain tissue. Although the study will not change the current anesthesia procedure, there is enough data to suggest a potential effect of N<sub>2</sub>O + ISO to the brain tissues.

[http://www.eurekalert.org/pub\\_releases/2012-12/bmj-imw121212.php](http://www.eurekalert.org/pub_releases/2012-12/bmj-imw121212.php)

## **Intense mind wandering could account for 'substantial proportion' of road crashes**

### ***And 13 percent of those crashes are due to 'disturbing' thoughts***

People whose minds wander whilst driving, especially when intense, are significantly more likely to be responsible for a crash and are threatening safety on the roads, warns a study in the Christmas issue published on bmj.com today. The term "mind wandering" has been coined to describe thinking unrelated to the task at hand. It happens most often at rest or during repetitive tasks. All drivers experience occasional drifting of their minds towards internal thoughts, a temporary "zoning out" that might dangerously distract them from the road. External distractions (such as from mobile phones) are known to be linked with crashes, but inattention arising from internal distractions (such as worries) is still poorly understood in the context of road safety.

A team of researchers from France therefore wanted to see if mind wandering would increase the risk of being responsible for a crash.

They interviewed 955 drivers injured in a motor vehicle crash attending the emergency department at Bordeaux University Hospital between April 2010 and August 2011. All participants were 18 years or older.

Patients were asked to describe their thought content just before the crash. Researchers also assessed how disruptive/distracting the thought was. Mitigating factors considered to reduce driver responsibility, such as road environment, traffic conditions, traffic rule obedience and difficulty of the driving task were also taken into account.

Finally, blood alcohol level was tested as well as the driver's emotional state just before the crash. They classified 453 (47%) drivers as responsible for the crash and 502 (53%) as not responsible. Over half (52%) reported some mind wandering just before the crash, and its content was highly disrupting / distracting (defined as intense mind wandering) in 121 (13%).

Intense mind wandering was associated with greater responsibility for a crash - 17% (78 of 453 crashes in which the driver was thought to be responsible) compared with 9% (43 of 502 crashes in which the driver was not thought to be responsible).

This association remained after adjusting for other confounding factors that could have affected the results. The authors conclude that the association between intense mind wandering and crashing "could stem from a risky decoupling of attention from online perception, making the driver prone to overlook hazards and to make more errors during driving."



They add that this study could lead to new interventions to help drivers by detecting periods of inattention. "Detecting those lapses can therefore provide an opportunity to further decrease the toll of road injury."

<http://phys.org/news/2012-12-earth-mantel-penetrated-metallic-blobs.html>

### **New study suggests Earth's lower mantle penetrated by metallic blobs**

*Researchers have found that molten iron is able to penetrate into rock samples in a unique way*

Phys.org - Researchers from Yale University have found that molten iron is able to penetrate into rock samples in a unique way under certain conditions. Geophysicist Shun-ichiro Karato and student Kazuhiko Otsuka together have found that when molten iron is brought into contact with magnesium-iron oxide crystals under high pressures and temperatures, metal blobs form inside the crystals – suggesting that it might be possible that the Earth's lower mantle might consist of a similar metal heavy material. They present their findings in a joint paper published in the journal Nature.

The Earth, as most science students know, has three main parts: the crust, the mantle and the core. Scientists learn more about the makeup of the mantle and core by studying seismic waves sent through them, and studying the way electrical signals change as they pass through the different layers. Studies done over the years have led researchers to believe that the lower part of the mantle has been imbued with iron from the core. But, other research has shown that simple diffusion would not be sufficient to account for the amount of metal that appears to exist there, nor would other known infiltration processes. In this new research, the team suggests it got there by a means never before seen.

The researchers created a high pressure, heated environment where they caused samples of molten iron to come into contact with crystals of magnesium-iron oxide. After just a few minutes they noted that iron rich blobs of liquid began penetrating into the crystals. In their lab the penetration was just 100 micrometers, but the two suggest that in a much larger environment, such as where the Earth's core meets the mantle, such penetration could extend to 100 kilometers, offering an explanation of why the lower mantle appears to have so much iron in it. They suggest that the blobs form due to an instability that occurs in the concentration gradient of iron oxide in the crystal.

This new research may also help to explain what appear to be dense layers observed in other planets as well. But, because magnesium-iron oxide is rather rare in the Earth's mantle, new research will focus on finding other minerals that behave in the same way when exposed to molten iron.

More information: Deep penetration of molten iron into the mantle caused by a morphological instability, Nature 492, 243–246 (13 December 2012) doi:10.1038/nature11663

#### **Abstract**

*The core–mantle boundary of Earth is a region where iron-rich liquids interact with oxides and silicates in the mantle. Iron enrichment may occur at the bottom of the mantle, leading to low seismic-wave velocities and high electrical conductivity, but plausible physical processes of iron enrichment have not been suggested. Diffusion-controlled iron enrichment is inefficient because it is too slow<sup>6</sup>, although the diffusion can be fast enough along grain boundaries for some elements. More fundamentally, experimental studies and geophysical observations show that the core is under-saturated with oxygen, implying that the mantle next to the core should be depleted in FeO. Here we show that (Mg,Fe)O in contact with iron-rich liquids leads to a morphological instability, causing blobs of iron-rich liquid to penetrate the oxide. This morphological instability is generated by the chemical potential gradient between two materials when they are not in bulk chemical equilibrium, and should be a common process in Earth's interior. Iron-rich melt could be transported 50 to 100 kilometres away from the core–mantle boundary by this mechanism, providing an explanation for the iron-rich regions in the mantle.*

<http://blogs.scientificamerican.com/guest-blog/2012/12/13/are-western-chimpanzees-a-new-species-of-pan/>

### **Are Western Chimpanzees a New Species of Pan?**

*Western chimpanzees are currently understood as one of four subspecies of chimpanzee*

By Cadell Last | December 13, 2012

What if I told you there were populations of chimpanzees that made spears to hunt, lived in caves, and loved playing in water? These are behaviors usually associated with ancient humans, not chimpanzees. However, recent research has revealed that there are populations of western chimpanzees (*Pan troglodytes verus*) that engage in all of these behaviours, and it is challenging our current understanding of chimpanzee taxonomy. In other words, they may not be chimpanzees!

Western chimpanzees are currently understood as one of four subspecies of chimpanzee. The other three subspecies are eastern chimpanzees (*Pan troglodytes schweinfurthii*), central chimpanzees (*Pan troglodytes troglodytes*), and Cameroon-Nigeria chimpanzees (*Pan troglodytes ellioti*). Collectively, these subspecies are members of one of the most well-studied wild animals on the planet. There are currently several field sites across Africa where long-term, continuous behavioural and ecological studies have been conducted (e.g.,

Whiten et al., 1999). Through these studies, we now have a detailed understanding of our closest relatives' social structure, mental capacity, and culture. The more we understand about our closest relatives, the more we are forced to relegate our differences from them to human-constructed continuums of complexity. However, researchers are now realizing that there is incredible behavioral, ecological, and genetic diversity within chimpanzees, that was previously unknown.

### **The East African chimp bias**

Until recently, scientists knew very little about chimpanzee subspecies variation. An overwhelming majority of wild field studies focused on eastern chimpanzees (*Pan troglodytes schweinfurthii*), the subspecies of chimpanzee first studied by Jane Goodall at Gombe in Tanzania (e.g., Goodall, 1962; Goodall, 1967; Goodall, 1968). Studies of this subspecies primarily informed our scientific understanding of wild chimpanzee behaviour and ecology. Over the decades, this resulted in what primatologist, Dr. Jill Pruetz, called an "East African chimp bias" (Pruetz, 2009). This means that eastern chimpanzee behaviour is typically used to represent normative chimpanzee behaviour. Researchers have shown that western chimpanzees do not fit the eastern chimpanzee stereotype (e.g., Humle & Matsuzawa, 2002; Boesch, 2009; Pruetz & Bertolani, 2009; Bogart & Pruetz, 2011).

One of the major causes of this initial bias was habituation. Habituation is the process of conditioning an animal to behave neutrally to a human's presence, and as I discovered on two recent field surveys in Cameroon, behavioral studies are impossible to conduct on unhabituated populations of chimpanzees. However, the process of habituation presented (and still presents) primatologists with logistical and ethical concerns. Logistically, habituation is difficult because chimpanzees lose their fear of our presence only after several years of repeated neutral contact with researchers (Fedigan, 2010). Habituation presents ethical concerns because humans in general are a threat to chimpanzee existence in the wild (Kondgen et al., 2008; Hughes et al., 2011). It is evolutionarily advantageous for them to avoid us, as opposed to tolerate us (Fedigan, 2010). Despite all of these problems, eastern chimpanzees were the first subspecies habituated, while most other populations remained unhabituated, thus creating the East African chimp bias.

### **What's so different?**

Recent primatological research on western chimpanzees has revealed behaviors never before observed in other subspecies. This seems to be particularly evident in the behaviour of the Fongoli chimpanzees in Senegal. They live in a woodland-savanna mosaic environment, which is atypical because most known populations of chimpanzee live in a forested environment. They have been observed to use caves as places to socialize and sleep (Pruetz, 2007), predict movement of fire (Pruetz & LaDuke, 2009), construct spears to hunt other primates (Pruetz & Bertolani, 2007), share plant foods (Pruetz, 2009), feed disproportionately on termites compared to other populations (Bogart & Pruetz, 2011), travel and forage at night (Pruetz & Bertolani, 2009), soak themselves, and play in water (Pruetz & Bertolani, 2009). These discoveries have forced scientists to rethink behavioral variation among chimpanzee subspecies because eastern chimpanzees have never been observed to behave in any of those ways (Pruetz, 2009). Furthermore, researchers at other sites in West Africa have also collected data bolstering the claim that western chimpanzee behavior is unlike eastern chimpanzee behavior (e.g., Whiten et al., 2001; Boesch, 2009; Stumpf & Boesch, 2010).

So, are western chimpanzees so different from eastern chimpanzees that they should be classified as a separate species of the genus *Pan*? Are they more different from eastern chimpanzees than they are from other closely related primates, such as bonobos? It is hard to quantify behavioral differences, but it appears as though western and eastern chimpanzees are more behaviorally similar to each other than eastern chimpanzees are to bonobos (Pruetz, 2009). Also, it is still unclear to what extent the ecological differences between western and eastern chimpanzee habitats are causing these behavioural differences. Understanding these questions will require future behavioral studies but current genetic evidence may help us better understand the causes of chimpanzee variation.

Genetic evidence indicates that western chimpanzees have been separated from the other chimpanzee subspecies for almost 500,000 years (Gonder et al. 2011). In contrast, central and eastern chimpanzees may have consisted of a single population as recently as 100,000 years ago (Gonder et al., 2011). Other genetic studies have confirmed that central and eastern chimpanzee populations are more closely related to each other than they are to western chimpanzees (Becquet et al., 2007). To put those numbers in perspective, bonobos (*Pan paniscus*) diverged from all chimpanzee subspecies only ~875,000 years ago (Won & Hey, 2004). Furthermore, research has revealed that subspecies genetic differences between western and central chimpanzees are much stronger than seen between any human populations (Fischer et al., 2004). This could indicate that there has been strong directional selection and/or genetic drift within western chimpanzee

populations over the past 500,000 years. Is that enough genetic divergence and difference to reclassify *Pan troglodytes verus*?

### A new Pan?

Whether western chimpanzees should be considered a different species within the genus *Pan* now seems to be largely dependent on definition. There are several different ways to classify a species. Some researchers define a species as any organisms that can actually, or potentially interbreed in the wild and produce fertile offspring. Under this definition, western chimpanzees would not be reclassified because all subspecies of chimpanzee can interbreed and produce fertile offspring, even though they are reproductively isolated in the wild. However, species are not always classified under this definition. Species can also be classified based on similarities and differences in DNA, morphology, and ecological niche. Current behavioral, ecological, and genetic data have revealed that there is an incredible and unexpected amount of chimpanzee subspecies variation that may require us to restructure African great ape taxonomy. But regardless of whether researchers decide to reclassify western chimpanzees, better understanding of chimpanzee variation has enabled us to gain new insight into our closest relatives, and explore our origins as a species in greater detail. Spear-making, cave-dwelling, water-loving western chimpanzees offer us a new opportunity to understand early human evolution. Let's continue to explore.

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<http://bit.ly/Uz7N2t>

## Overeating now bigger global problem than lack of food

*The largest ever study into the state of the world's health has revealed that, for the first time, the number of years of healthy living lost as a result of people eating too much outweigh the number lost by people eating too little.*

17:40 13 December 2012 by Jessica Hamzelou

The Global Burden of Disease report – a massive research effort involving almost 500 scientists in 50 countries – also concludes that we have finally got a handle on some common infectious diseases, helping to save millions of children from early deaths. But collectively we are spending more of our lives living in poor health and with disability.

"The Global Burden of Disease 2010 is the most comprehensive assessment of human health in the history of medicine," says Richard Horton, editor of *The Lancet*, in which the report will be published. "It provides insights into human health that are comparable in scope and depth to the sequencing of the human genome." The report assessed the prevalence of diseases and causes of death across the globe in 2010, and compared these to data collected in 1990 to identify any trends.

For the first time on a global scale, being overweight has become more of a health problem than lack of nutrition. In 1990, undernutrition was the leading cause of disease burden, measured as the number of years of healthy life an average person could expect to lose as a result of illness or early death. Back then, a high body-mass index, or BMI, was ranked tenth. Now, undernutrition has dropped to eighth place, while BMI has risen to become the sixth leading cause of disease burden.

Too much to eat

"A greater amount of disease burden has occurred because people are fat and have too much to eat, as opposed to having too little to eat," says Alan Lopez at the University of Queensland in Brisbane, Australia, who worked on the study.

Being overweight can hike a person's blood pressure and cause stroke and heart disease; together, these two conditions are responsible for a quarter of all deaths. And the problem isn't limited to the west – the Middle East is one region that is seeing significant increases in BMI.

But while more of us may be overweight, we are also living longer. In some countries, the change has been huge – the Maldives, for example, has seen an increase in life expectancy of almost 30 years since the 1970s. Rural health programmes have also contributed to big improvements in countries including Bangladesh and Iran.

"There has been a lot of progress," says Majid Ezzati at Imperial College London, who led part of the study investigating the risk factors of disease. "These are countries that have implemented programmes in large regions and nationwide to get interventions to the people that really need them."

Progress in eliminating the causes of early childhood death – mainly infections, diarrhoea and birth problems – has been astounding. The rate of death in the under-5s has dropped by 60 per cent since 1990.

High mortality

Sub-Saharan Africa is still experiencing high levels of mortality from infectious diseases such as HIV and malaria, yet globally deaths from infectious diseases have dropped. In fact, we are more likely to die from non-infectious diseases – especially those caused by being overweight.

Looking forward, obesity and the use of tobacco and alcohol are obvious targets for health policy change. But it is also important to focus on healthy ageing.

"The large burden [of disease] related to disability was a surprise," says Christopher Murray at the University of Washington in Seattle. "There's been a focus on mortality, but there's a huge volume [of disease burden] related to things that don't really kill you."

Musculoskeletal disorders – such as neck and back pain – dominate this category, as do mental disorders and substance abuse.

There's a need to improve awareness of these chronic conditions in the developing world, says Irene Agyepong at the University of Ghana in Accra, who was not involved in the study. "The kind of awareness we have in the western world is not there in the south," she says. "We have to focus on it now rather than wait until it is upon us, like the HIV AIDS epidemic is on us."

<http://www.wired.com/wiredscience/2012/12/stroke-priming/>

## Preparing the Brain for a Stroke Before It Occurs

*Priming the brain to sprout new blood vessels before a stroke occurs could reduce the severity and improve the patients' chances of recovering afterward, according to new research.*

By Brian Mossop

“They [might still] get the stroke, but it’s only half as bad and they may in fact recover,” said Jeff Dunn, Director of the Experimental Imaging Center at the University of Calgary. “I think that’s pretty exciting.” Fifteen million people suffer a stroke globally each year (.pdf) according to the World Health Organization, leaving many permanently disabled, or worse. Stroke occurs when fats or blood clots clog a mid-sized blood vessel, restricting blood flow, oxygen and nutrients to our sensitive gray and white matter. If the blockage lasts long enough, brain cells can start to die. Dunn has studied the protective effect of new blood vessel growth on the brain for years. Several years ago he discovered that when an animal lives at altitude, the oxygen partial pressure - a measure of healthy blood supply to a tissue - increases. Presumably, he thought, the boosted oxygen pressure, and therefore blood supply, was due to new vessels forming in the brain.

In a study published in PLoS ONE in September, Dunn’s team found evidence to support their suspicions by raising two groups of rats in different oxygen levels. One of the groups of rats lived at the natural atmospheric pressure of Calgary. They raised another group in a cage with half the normal atmospheric pressure and a lower oxygen percentage, equivalent to a rat cage lifted 3 miles higher.

After three weeks, the high-altitude rats had, on average, 30 percent more small blood vessels in their brains compared to their counterparts. The scientists then induced strokes in the rats by restricting blood flow and oxygen delivery to the brain and found that the high-altitude rats were more resistant to the negative effects of stroke, showing around half as much brain cell death and significantly reduced inflammation. They maintained motor functions, such as being able to peel a piece of sticky tape off their feet after the stroke, that were more or less lost by the rats raised at lower altitude.

Dunn believes that the brain, while strapped for blood supply in a low-oxygen, high-altitude environment, ratcheted up its production of a protein that helps cause new blood vessels to form. Dunn’s theory is that a kind of interconnected web of blood vessels forms within the brain. So when one mid-sized vessel gets clogged, it can rely on its partner vessels to provide an alternate path for the blood and oxygen.

While Dunn’s results are promising in the short-term, stroke researcher Donna Ferriero, chief physician at the University of California Benioff Children’s Hospital, says the researchers may have jumped the gun in determining how the animal was affected by the stroke; ideally they should check how the rats are doing a few weeks later, rather than immediately after the stroke.

Dunn hopes that in time, his findings in animals could benefit patients who come into the emergency room suffering from transient ischemic attacks (TIA), a condition where blood flow is only temporarily shut off from the brain, causing stroke-like symptoms. “These people with TIAs, many of them come back with a major stroke within the next week or two,” Dunn said. “If we could ... treat them in a way that protects them if they have a major stroke, well that would be huge.” Even for patients with a high risk of experiencing a stroke in the near future, preparing them by reducing the amount of oxygen they breathe isn’t the best approach, Dunn acknowledged. But it may be possible to use drugs to get the same effects as reduced oxygen.

Ferriero agreed that a number of animal studies have shown that drugs can produce some of the same protective effects by increasing blood vessel formation. And a recent Phase 1 clinical trial in newborn humans supports Dunn’s hypothesis as well. However, current data for the same treatment in adults is not as encouraging.

With further research, it’s at least possible that doctors could one day use such a treatment on high-risk patients so that their brains are primed with new vessels in case something worse happens down the line.

Citation: Dunn JF, Wu Y, Zhao Z, Srinivasan S, Natah SS (2012) Training the Brain to Survive Stroke. PLoS ONE 7(9): e45108. doi:10.1371/journal.pone.0045108

<http://www.sciencedaily.com/releases/2012/12/121213145257.htm>

## Predatory Fungi Are Listening for Worms, Then Devouring Prey

*Taking a closer look at how predatory fungi may be tapping into worm conversations to gain clues about their whereabouts*

For over 25 years, Paul Sternberg has been studying worms -- how they develop, why they sleep, and, more recently, how they communicate. Now, he has flipped the script a bit by taking a closer look at how predatory fungi may be tapping into worm conversations to gain clues about their whereabouts.

Nematodes, Sternberg's primary worm interest, are found in nearly every corner of the world and are one of the most abundant animals on the planet. Unsurprisingly, they have natural enemies, including numerous types of carnivorous fungi that build traps to catch their prey. Curious to see how nematophagous fungi might sense that

a meal is present without the sensory organs -- like eyes or noses -- that most predators use, Sternberg and Yen-Ping Hsueh, a postdoctoral scholar in biology at Caltech, started with a familiar tool: ascarosides. These are the chemical cues that nematodes use to "talk" to one another.

"If we think about it from an evolutionary perspective, whatever the worms are making that can be sensed by the nematophagous fungi must be very important to the worm -- otherwise, it's not worth the risk," explains Hsueh. "I thought that ascarosides perfectly fit this hypothesis."

In order to test their idea, the team first evaluated whether different ascarosides caused one of the most common nematode-trapping fungi species to start making a trap. Indeed, it responded by building sticky, web-like nets called adhesive networks, but only when it was nutrient-deprived. It takes a lot of energy for the fungi to build a trap, so they'll only do it if they are hungry and they sense that prey is nearby. Moreover, this ascaroside-induced response is conserved in three other closely related species. But, the researchers say, each of the four fungal species responded to different sets of ascarosides.

*Nematodes are trapped in the sticky web of a worm-eating fungus. (Credit: Sternberg*



*Lab / Caltech)*

"This fits with the idea that different types of predators might encounter different types of prey in nature, and also raises the possibility that fungi could 'read' the different dialects of each worm type," says Sternberg.

"What's cool is that we've shown the ability for a predator to eavesdrop on essential prey communication. The worms have to talk to each other using these chemicals, and the predator is listening in on it -- that's how it knows the worms are there."

Sternberg and Hsueh also tested a second type of fungus that uses a constricting ring to trap the worms, but it did not respond to the ascarosides. However, the team says that because they only tested a handful of the chemical cues, it's possible that they simply did not test the right ones for that type of fungus.

"Next, the focus is to really study the molecular mechanism in the fungi -- how does a fungus sense the ascarosides, and what are the downstream pathways that induce the trap formation," says Hsueh. "We are also interested in evolutionary question of why we see this ascaroside sensing in some types of fungi but not others."

In the long run, their findings may help improve methods for pest management. Some of these fungi are used for biocontrol to try and keep nematodes away from certain plant roots. Knowing more about what stimulates the organisms to make traps might allow for the development of better biocontrol preparations, says Sternberg. The full results of Sternberg and Hsueh's study can be found in the paper, "Nematode-trapping fungi eavesdrop on nematode pheromones," published in the journal *Current Biology*.

*Yen-Ping Hsueh, Parag Mahanti, Frank C. Schroeder, Paul W. Sternberg. Nematode-Trapping Fungi Eavesdrop on Nematode Pheromones. Current Biology, 2012; DOI: 10.1016/j.cub.2012.11.035*

<http://bit.ly/V1kMgQ>

### **Permian mass extinction triggered by humble microbe**

***AROUND 251 million years ago, over 90 per cent of the species on Earth suddenly went extinct.***

**14 December 2012 by Sara Reardon**

Their killer may not have been a devastating meteorite or a catastrophic volcanic eruption, but a humble microbe. The prevailing theory is that the mass extinction at the end of the Permian period was triggered by volcanic eruptions over a vast area of what is now Siberia. This led, among other things, to a dramatic rise in greenhouse gas emissions. But the scenario just doesn't fit the facts, says Daniel Rothman of the Massachusetts Institute of Technology. From his analysis of an end-Permian sediment sample from China, Rothman says carbon levels surged much too quickly for geological processes to be at work.

Microbes can generate carbon compounds that fast, though. When Rothman's group analysed the genome of *Methanosarcina* - a methanogen responsible for most of Earth's biogenic methane today - they discovered that the microbe gained this ability about 231 million years ago. The date was close to that of the mass extinction, but not close enough to suggest a link.

But *Methanosarcina* needs large amounts of nickel to produce methane quickly. When the team went back to their sediment cores, they discovered that nickel levels spiked almost exactly 251 million years ago - probably because the Siberian lavas were rich in the metal. That suggests *Methanosarcina* did trigger the extinction, Rothman told the American Geophysical Union meeting in San Francisco last week.

Other geologists remain to be convinced. "[But] it's a fascinating idea that the evolution of a new life form led to an extinction," says Anthony Barnosky of the University of California, Berkeley. Today's mass extinction of biodiversity is similar, says Barnosky, because it is largely driven by our species.



<http://www.scientificamerican.com/article.cfm?id=boys-and-girls-may-get-different-breast-milk>

## Boys and Girls May Get Different Breast Milk

*Milk composition differs based on a baby's sex and a mother's wealth*

By Marissa Fessenden

Mother's milk may be the first food, but it is not created equal. In humans and other mammals, researchers have found that milk composition changes depending on the infant's gender and on whether conditions are good or bad. Understanding those differences can give scientists insights into human evolution.

Researchers at Michigan State University and other institutions found that among 72 mothers in rural Kenya, women with sons generally gave richer milk (2.8 percent fat compared with 0.6 percent for daughters). Poor women, however, favored daughters with creamier milk (2.6 versus 2.3 percent). These findings, published in the American Journal of Physical Anthropology in September, echo previous work that showed milk composition varying with infant gender in gray seals and red deer and with infant gender and the mother's condition in rhesus macaques. The new study also follows findings that affluent, well-nourished moms in Massachusetts produced more energy-dense milk for male infants.

Together the studies provide support for a 40-year-old theory in evolutionary biology. The Trivers-Willard hypothesis states that natural selection favors parental investment in daughters when times are hard and in sons when times are easy. The imbalance should be greatest in polygamous societies, in which men can father offspring with multiple wives, such as the Kenyan villages. In those societies, a son can grow to be a strong, popular male with many wives and children, or he can end up with neither. Well-off parents who can afford to invest in sons should do so because their gamble could give them many grandchildren. Conversely, poor parents should not heavily invest in sons because it is unlikely to pay off—their offspring start at the bottom of the socioeconomic ladder. For those families, daughters are a safer bet because as long as they survive to adulthood, they are likely to produce young.

The new study is “exciting and enthralling,” says Robert Trivers, an evolutionary biologist at Rutgers University and co-author of the hypothesis, who was not involved in the recent work. “It is a Trivers-Willard effect I wouldn't have the guts to predict.”

Even beyond fat and protein, other milk components might vary in humans, says Katie Hinde, an assistant professor in human evolutionary biology at Harvard University. She has found higher levels of cortisol, a hormone that regulates metabolism, in rhesus macaque milk for male infants. Her work shows that milk differences could change infant behavior and might affect growth and development. “Only half the story is what the mom's producing,” Hinde says. “The other [half] is how the infant uses the milk.” These findings could have implications for formula, which could be tweaked to optimize development for both boys and girls.

<http://www.sciencedaily.com/releases/2012/12/121214124020.htm>

## New Peatland Bacteria Feed On Greenhouse Gas and Excess Fertilizer

*Researchers have discovered new methane-consuming bacteria*

Researchers from Radboud University Nijmegen and B-WARE Research Centre have discovered new methane-consuming bacteria in the soil beneath the Brunssummerheide peatland reserve in Limburg, the Netherlands. Although the bacteria may be the result of environmental pollution, they are now consuming the harmful greenhouse gas. Applied and Environmental Microbiology has published the results in its December issue.

In the middle of the Brunssummerheide heathland reserve is a unique sloping peatland site with a great diversity of flora and fauna, such as the rare Bog Asphodel and the protected Northern Emerald dragonfly. The variety of landscape types within a small area means that it is vulnerable to water level and water quality changes. Dutch nature conservation association Vereniging Natuurmonumenten therefore wants to know how to best manage and protect the area, and called on the help of B-WARE Research Centre and Radboud University Nijmegen in 2008.

### Methane filter

Gijs van Dijk, the aquatic ecologist who took on the job, made a remarkable discovery. “I found high concentrations of methane, also called marsh gas, deep in the peat section, but detected none at the surface. The anaerobic peat soil was therefore effectively filtering out the methane -- but how?” This question has been solved by Katharina Ettwig, microbiologist at Radboud University Nijmegen.

### Soil research

Ettwig had already shown that special bacteria can oxidise methane anaerobically using nitrogen compounds such as nitrites and nitrates. “However, the process had never been seen outside the laboratory,” explains Ettwig. Following intensive soil and laboratory research, the methane filter in the Brunssummerheide peatland reserve was discovered to be the work of a new type of bacteria, a close relative to the previously-discovered

Methyloirabilis oxyfera. The bacteria make pure oxygen from nitrites and use this to 'burn' the methane, providing the bacteria with its source of energy.

### **Ideal conditions**

Every anaerobic peat soil contains methane. However, the groundwater in the Brunssummerheide peatland reserve also contains unusually high levels of nitrates, probably due to leaching from woodland and agricultural soils. This combination of methane, nitrate and the presence of oxygen in the Brunssummer peat provides ideal conditions for the Methyloirabilis bacteria. The bacteria are therefore already found in methane and nitrate-rich soils: nature conservationists do not need to introduce them. Natuurmonumenten will therefore mainly use this information to monitor groundwater pollution and, where possible, to tackle it at the source.

### **Applications for methane-eaters**

The researchers are currently investigating whether the global increase in nitrogen pollution is also reducing methane emissions in other ecosystems. They are also looking into the cell biology and biochemistry of the bacteria to find out if it has any practical applications, such as in water treatment. The Nijmegen Institute for Water and Wetland Research (IWWR) research group has a great deal of experience in cultivating, studying and finding applications for slow-growing, anaerobic bacteria. During previous joint research projects, they discovered the anammox bacteria and the methane-consuming volcano bacteria.

*Baoli Zhu, Gijs van Dijk, Christian Fritz, Alfons J. P. Smolders, Arjan Pol, Mike S. M. Jetten, Katharina F. Ettwig. Anaerobic Oxidization of Methane in a Minerotrophic Peatland: Enrichment of Nitrite-Dependent Methane-Oxidizing Bacteria. Applied and Environmental Microbiology, 2012; DOI: 10.1128/AEM.02102-12*

<http://www.sciencedaily.com/releases/2012/12/121214190951.htm?>

## **Flesh-Eating Fungus Responsible for Five Deaths in Wake of Massive Tornado**

*A fast growing, flesh-eating fungus killed 5 people following a massive tornado*

A fast growing, flesh-eating fungus killed 5 people following a massive tornado that devastated Joplin, Mo., according to two new studies based on genomic sequencing by the Translational Genomics Research Institute (TGen) and the U.S. Centers for Disease Control and Prevention (CDC).

Health officials should be aware of infections caused by the fungus Apophysomyces, according to the studies, which tracked 13 people infected by the pathogen during the Class EF-5 tornado -- the most powerful category -- whose 200-plus mph winds plowed through Joplin on May 22, 2011, initially killing 160 and injuring more than 1,000.

The common fungus -- which lives in soil, wood or water -- usually has no effect on people. But once it is introduced deep into the body through a blunt trauma puncture wound, it can grow quickly if the proper medical response is not immediate, the studies said. Five of the 13 people infected through injuries suffered during the Joplin tornado died within two weeks.

"Increased awareness of fungi as a cause of necrotizing soft-tissue infections after a natural disaster is warranted ... since early treatment may improve outcomes," concluded one study published Dec. 6 in The New England Journal of Medicine.

Using whole genome sequencing, which decoded the billions of chemical letters in the fungus' DNA, TGen scientists concluded that the Joplin infections represented the largest documented cluster of Apophysomyces infections, according to a study published Nov. 27 in the journal PLOS One.

"This is one of the most severe fungal infections that anyone's ever seen," said David Engelthaler, Director of Programs and Operations for TGen's Pathogen Genomics Division. Engelthaler was the senior author of the PLOS One study, and a contributing author of the NEJM study.

"We're able to apply the latest in science and technology to explore these strange and dangerous pathogens, like we've never been able to before," said Engelthaler, adding that this is the latest in a series of collaborations between CDC and TGen. "This is the first peek into the genome of this dangerous fungus."

Dr. Benjamin Park, chief of the Epidemiology Team at the CDC's Mycotic Diseases Branch, said the victims were infected when their injuries from the tornado were contaminated with debris from the storm, including gravel, wood and soil, as well as the aerosolized fungus.

Without the multiple and deep wounds caused by the storm, cases involving fungal infection are rare, said Dr. Park, the senior author of the NEJM study and a contributing author of the PLOS One study. "A typical hospital might normally see one case in a year."

Engelthaler said Apophysomyces infections rapidly ravage the body, quickly sealing off capillaries, shutting off the blood supply and leaving tissue to rot. Physicians try to get ahead of the infection by surgically removing sections of dead, damaged or infected tissue, a process called debridement.

For example, Engelthaler said, one victim who suffered a deep wound to the upper right chest required a new titanium rib cage after the fungus rapidly destroyed skin and bones.

"It's unlike anything you've ever seen before," said Engelthaler, a former State of Arizona Epidemiologist and former Arizona Biodefense Coordinator. "It's unreal. It looks like there is no way this person can be alive." The studies show the need for rapid and accurate identification of the exact mold causing an infection, since only two FDA-approved drugs -- amphotericin B and posaconazole -- are commonly used against mucormycetes, the group of molds that includes Apophysomyces and causes mucormycosis.

"It is not known whether the outcomes for these case patients would have been different if mucormycete-active agents had been used initially," said the NEJM study. "The timely diagnosis of mucormycosis is essential for guiding therapy, because the early initiation of appropriate anti-fungal medication and aggressive surgical debridement are associated with improved outcomes." Both the NEJM and PLOS One studies said whole genome sequencing could lead to better diagnosis and a better understanding of this pathogen.

TGen's DNA sequencing identified Apophysomyces in all 13 of the Joplin cases. The DNA analysis also established that several strains of Apophysomyces were involved in the outbreak, giving scientists further clues that this fungus was well established in the area, and probably had been so for a long time.

"These disasters put us at risk for exposure to organisms that are around us, but don't normally cause disease," Engelthaler said. "There's clearly an entire world out there that we're not seeing on a regular basis. It takes a severe event like this tornado for us to come face-to-face with some of the more dangerous pathogens out there."

Marion A. Kainer, David R. Reagan, Duc B. Nguyen, Andrew D. Wiese, Matthew E. Wise, Jennifer Ward, Benjamin J. Park, Meredith L. Kanago, Jane Baumbblatt, Melissa K. Schaefer, Brynn E. Berger, Ellyn P. Marder, Jea-Young Min, John R. Dunn, Rachel M. Smith, John Dreyzehner, Timothy F. Jones. *Fungal Infections Associated with Contaminated Methylprednisolone in Tennessee*. *New England Journal of Medicine*, 2012; 367 (23): 2194 DOI: 10.1056/NEJMoa1212972

<http://blog.longnow.org/02012/12/14/aspirin-a-3500-year-old-remedy/>?

### **Aspirin: A 3,500-Year Old Remedy**

*Aspirin is not only a miraculous cure-all; it's also an ancient one.*

In its purified chemical form, aspirin (or salicylic acid) is only a little over 100 years old. But the compound is also found in several plants – and in this form, it has been used for over 3,500 years.

Its pain-reducing and anti-inflammatory properties were already known to Hippocrates, who found salicylic acid in the leaves and bark of willow trees and used it, among other things, to ease the pain of childbirth. He most likely learned of this medicine from ancient Egyptian and Sumerian medical texts, which recommend the use of willow leaves for treating inflammation (Mackowiak 2000).

The healing potential of willows was recognized the world over – from the Roman Empire to ancient China, and, in the new world, among Native American tribes as well. In Europe, too, willow leaves were used medicinally, until, in the late nineteenth century, the Bayer pharmaceutical company figured out how to manufacture salicylic acid in a laboratory and market it for mass consumption (The Naked Scientist).

Today, modern medical research may have given us renewed insight into the workings and benefits of this over-the-counter pill, but aspirin is ultimately the product of a history that spans several millennia.

[http://www.eurekalert.org/pub\\_releases/2012-12/uoea-pw121312.php](http://www.eurekalert.org/pub_releases/2012-12/uoea-pw121312.php)

### **'Missing' polar weather systems could impact climate predictions**

*Intense but small-scale polar storms could make a big difference to climate predictions according to new research from the University of East Anglia and the University of Massachusetts.*

Difficult-to-forecast polar mesoscale storms occur frequently over the polar seas, however they are missing in most climate models.

Research published today in *Nature Geoscience* shows that their inclusion could paint a different picture of climate change in years to come.

Polar mesoscale storms are capable of producing hurricane-strength winds which cool the ocean and lead to changes in its circulation.

Prof Ian Renfrew, from UEA's School of Environmental Sciences, said: "These polar lows are typically under 500 km in diameter and over within 24-36 hours. They're difficult to predict, but we have shown they play an important role in driving large-scale ocean circulation.

"There are hundreds of them a year in the North Atlantic, and dozens of strong ones. They create a lot of stormy weather, strong winds and snowfall – particularly over Norway, Iceland, and Canada, and occasionally over Britain, such as in 2003 when a massive dump of snow brought the M11 to a standstill for 24 hours.

"We have shown that adding polar storms into computer-generated models of the ocean results in significant changes in ocean circulation - including an increase in heat travelling north in the Atlantic Ocean and more overturning in the Sub-polar seas.

"At present, climate models don't have a high enough resolution to account for these small-scale polar lows.



"As Arctic Sea ice continues to retreat, polar lows are likely to migrate further north, which could have consequences for the 'thermohaline' or northward ocean circulation – potentially leading to it weakening." Alan Condrón from the University of Massachusetts said: "By simulating polar lows, we find that the area of the ocean that becomes denser and sinks each year increases and causes the amount of heat being transported towards Europe to intensify.

"The fact that climate models are not simulating these storms is a real problem because these models will incorrectly predict how much heat is being moved northward towards the poles. This will make it very difficult to reliably predict how the climate of Europe and North America will change in the near-future."

Prof Renfrew added: "Climate models are always improving, and there is a trade-off between the resolution of the model, the complexity of the model, and the number of simulations you can carry out. Our work suggests we should put some more effort into resolving such storms."

*'The impact of polar mesoscale storms on Northeast Atlantic ocean circulation' by Alan Condrón from the University of Massachusetts (US) and Ian Renfrew from UEA (UK), is published in Nature Geoscience on December 16, 2012.*

<http://www.sciencedaily.com/releases/2012/12/121216132501.htm>

### **Action by 2020 Key for Limiting Climate Change**

***Limiting climate change to target levels will become much more difficult to achieve, and more expensive, if action is not taken soon, according to a new analysis from IIASA, ETH Zurich, and NCAR.***

The new paper, published today in Nature Climate Change, explores technological, policy, and social changes that would need to take place in the near term in order to keep global average temperature from rising above 2°C, a target supported by more than 190 countries as a global limit to avoid dangerous climate change. This study for the first time comprehensively quantifies the costs and risks of greenhouse gas emissions surpassing critical thresholds by 2020. The findings of the study are particularly important given the failure of the recent climate negotiations in Doha to decide to increase mitigation action before 2020.

The authors show that the 2°C target could still be reached even if greenhouse gas emissions are not reduced before 2020, but only at very high cost, with higher climate risks, and under exceedingly optimistic assumptions about future technologies. The more emissions are reduced in the near term, the more options will be available in the long run and, by extension, the cheaper it will be to reach international climate targets.

"We wanted to know what needs to be done by 2020 in order to be able to keep global warming below two degrees Celsius for the entire twenty-first century," says Joeri Rogelj, lead author of the paper and researcher at ETH Zurich. The team of researchers analyzed a large array of potential scenarios for limiting global temperature rise to 2 °C above preindustrial levels, a target set by international climate agreements.

Projections based on current national emissions pledges suggest that global carbon dioxide equivalent (CO<sub>2</sub>e) emissions will reach 55 gigatons (billion metric tons, Gt) or more per year in 2020, up from approximately 50 Gt today. At such levels, it would still be possible to reach the 2°C target in the long term, though it would be more difficult and expensive than if near-term emissions were lower.

For instance, nuclear power would need to remain on the table as a mitigation option, or people would need to quickly adopt advanced technology strategies, including electric vehicles and highly efficient energy end-use technologies such as appliances, buildings, and transportation. Meanwhile, coal-fired power plants would need to be rapidly shut down and replaced with other energy sources. IIASA Energy Program Leader Keywan Riahi, who also worked on the study, says, "You would need to shut down a coal power plant each week for ten years if you still wanted to reach the two-degree Celsius target."

"If we want to keep as many options open as possible, we should aim to reduce global emissions to 41 to 47 gigatons of carbon dioxide equivalent per year by 2020," says Rogelj. According to the study, the only way to meet the long-term temperature target without carbon capture and storage is to ensure that emissions fall within this near-term range.

"What we do over the next eight years really determines the feasibility and choices that we have in the long term," says Riahi. "Some of these options for policies and technological change are still choices, such as phasing out nuclear power. We lose these choices if we overshoot certain thresholds."

The study goes beyond previous analyses by directly assessing how high emissions in 2020 can go before the long-term target of 2 °C is no longer attainable. "Under some conditions, the two-degree target is feasible even if we don't reduce emissions at all by 2020," says co-author Brian O'Neill, of the National Center for Atmospheric Research in Boulder, Colorado. "But if we allow for the possibility that some technologies may not pan out, or are overly costly or have undesirable consequences, then emissions reductions have to start this decade."

"Our analysis shows that we are very dependent on key technologies like carbon capture and storage and on land-consuming measures like afforestation and the cultivation of crops for biofuel production," says Rogelj. "If

we want to become less dependent on massive implementation of these technologies to make it below two degrees Celsius, we need to reduce emissions by 2020 and use energy more efficiently."

The study highlights the importance of reducing energy demand and improving efficiency as perhaps the most effective way to mitigate climate change this decade, echoing previous work from IIASA and others (Global Energy Assessment, 2012). In scenarios with lower energy demand growth, the researchers find a much greater chance that global temperatures would not rise more than 2 °C, with much more flexibility in the methods and technologies required to reduce greenhouse gases.

"Fundamentally, it's a question of how much society is willing to risk," says IIASA energy researcher David McCollum, another study co-author. "It's certainly easier for us to push the climate problem off for a little while longer, but if we do that, then we risk that certain mitigation options may not ultimately be available in the long run. What's more, from the perspective of the global climate system, continuing to pump high levels of emissions into the atmosphere over the next decade only increases the risk that we will overshoot the two-degree target."

Joeri Rogelj, David L. McCollum, Brian C. O'Neill, Keywan Riahi. 2020 emissions levels required to limit warming to below 2 °C. *Nature Climate Change*, 2012; DOI: 10.1038/NCLIMATE1758

[http://www.eurekalert.org/pub\\_releases/2012-12/apa-gng121412.php](http://www.eurekalert.org/pub_releases/2012-12/apa-gng121412.php)

### **Greed, not generosity, more likely to be 'paid forward'**

*With money or work, people are more likely to look out for themselves*

WASHINGTON - Paying it forward - a popular expression for extending generosity to others after someone has been generous to you - is a heartwarming concept, but it is less common than repaying greed with greed, according to new research published by the American Psychological Association.

"The idea of paying it forward is this cascade of goodwill will turn into a utopia with everyone helping everyone," said lead researcher Kurt Gray, PhD. "Unfortunately, greed or looking out for ourselves is more powerful than true acts of generosity."

The study, published online in APA's *Journal of Experimental Psychology: General*, is the first systematic investigation of paying forward generosity, equality or greed, according to the authors.

"The bulk of the scientific research on this concept has focused on good behavior, and we wondered what would happen when you looked at the entire gamut of human behaviors," said Gray, an assistant professor of social psychology at the University of North Carolina-Chapel Hill, who conducted the study with researchers at Harvard University.

In five experiments involving money or work, participants who received an act of generosity didn't pay generosity forward any more than those who had been treated equally. But participants who had been the victims of greed were more likely to pay greed forward to a future recipient, creating a negative chain reaction. Women and men showed the same levels of generosity and greed in the study.

In one experiment, researchers recruited 100 people from subway stations and tourist areas in Cambridge, Mass., to play an economic game. They told participants that someone had split \$6 with them and then gave them an envelope that contained the entire \$6 for a generous split, \$3 for an equal split, or nothing for a greedy split. The participants then received an additional \$6 that they could split in another envelope with a future recipient, essentially paying it forward.

Receiving a generous split didn't prompt any greater generosity than receiving equal treatment, but people who received nothing in the first envelope were more likely to put little or nothing in the second envelope, depriving future recipients because of the greed they had experienced. The average amount paid forward by participants who received a greedy split was \$1.32, well below an equal split of \$3.

The results confirmed the researchers' hypothesis that greed would prevail because negative stimuli have more powerful effects on thoughts and actions than positive stimuli. Focusing on the negative may cause unhappiness, but it makes sense as an evolutionary survival skill, Gray said. "If there is a tiger nearby, you really have to take notice or you'll get eaten," he said. "If there is a beautiful sunset or delicious food, it's not a life-or-death situation."

The study also examined whether people would have similar reactions involving work rather than money. In one online experiment, researchers told 60 participants that four tasks needed to be completed, including two easy word association games and two boring, repetitive tasks that involved circling vowels in dense Italian text. They explained to the participants that someone had already split the work with them, leaving them the two fun tasks in a generous split, one fun task and one boring task in an equal split, or both boring tasks in a greedy split. The participants then had to complete those tasks and split an additional four tasks with a future recipient. The results were the same, with greed being paid forward more than generosity.

"We all like to think that being generous will influence others to treat someone nicely, but it doesn't automatically create a chain of goodwill," said Gray. "To create chains of positive behavior, people should focus less on performing random acts of generosity and more on treating others equally—while refraining from random acts of greed."

*Article: "Paying It Forward: Generalized Reciprocity and the Limits of Generosity," Kurt Gray, PhD, University of North Carolina-Chapel Hill; Adrian F. Ward, MA; and Michael I. Norton, PhD, Harvard University; Journal of Experimental Psychology: General; online Dec. 17, 2012.*

*Full text of the article is available from the APA Public Affairs Office and at <http://www.apa.org/pubs/journals/releases/xge-ofp-gray.pdf>*

<http://www.bbc.co.uk/news/uk-england-merseyside-20732332>

### **Musical ear syndrome: The woman who constantly hears music**

***"Happy Birthday - every few minutes I'm wishing someone happy birthday - I hate that one."***

The song is one of several numbers Cath Gamester, 84, hears on a constant loop throughout the day. The grandmother from Liverpool has musical ear syndrome, where the sufferer has auditory hallucinations. Since it started in 2010, she said she had heard songs including God Save The Queen, Abide with me, You'll Never Walk Alone and Silent Night.

She said: "it just goes on and on and on, one song after another.

"It's a tenor, a man's voice and it's a nice voice, very strong, loud and there's like a background of music."

The rare condition affects about one in 10,000 people over 65 in the UK.

Often, the person is also suffering from tinnitus.

#### **'Musical hallucination'**

Mrs Gamester believes the songs were triggered by a course of anti-depressants she was prescribed after the death of her sister.

"I went to bed and when I woke up I heard music. I thought to myself it must be next door - he must be playing a record because it was going on and on.

"I went out the back door, I went out the front door, I went out to see if there was any music being played everywhere, I was thinking where is it coming from?"

Mrs Gamester said she sometimes vacuumed or told it to "shut up" in a bid to drown the noise out.

Dr Nick Warner, a psychiatrist who specialises in the elderly, said he usually dealt with "a couple of cases a year" connected to musical ear syndrome.

"When you get a musical hallucination it feels as if it's real, it feels as if there's a record player playing it or the artist is in the room or in the next-door room.

"As far as you're concerned probably everyone else ought to be able to hear it as well so it's very, very real."

Dr Warner said in the majority of cases he had encountered, people heard hymns and Christmas carols.

"On speculative terms, it could be that without knowing it, that person needs to hear something which is in some way reassuring to them."

#### **'Enjoy yourself'**

Despite no current cure to for the condition, Dr Warner said there are ways of helping people live with it.

"Some people have found that putting on other music enables them to take control over from the musical hallucinations.

"I think talking about it to other people probably helps, distracting yourself, doing as much as you possibly can."

Mrs Gamester said she had found her own way of accepting the hallucinations.

"I've worked out the fact that I should be glad it's not a serious illness.

"I would say to these poor people out there who are like me - don't let it worry you too much, get on with life and enjoy yourself as much as you can."