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## **Researchers discover human immune system has emergency backup plan**

***New research by scientists at the University of California, San Diego School of Medicine and Skaggs School of Pharmacy and Pharmaceutical Sciences reveals that the immune system has an effective backup plan to protect the body from infection when the "master regulator" of the body's innate immune system fails.***

The study appears in the December 19 online issue of the journal *Nature Immunology*.

The innate immune system defends the body against infections caused by bacteria and viruses, but also causes inflammation which, when uncontrolled, can contribute to chronic illnesses such as heart disease, arthritis, type 2 diabetes and cancer. A molecule known as nuclear factor kappa B (NF- $\kappa$ B) has been regarded as the "master regulator" of the body's innate immune response, receiving signals of injury or infection and activating genes for microbial killing and inflammation.

Led by Michael Karin, PhD, Distinguished Professor of Pharmacology, the UC San Diego team studied the immune function of laboratory mice in which genetic tools were used to block the pathway for NF- $\kappa$ B activation. While prevailing logic suggested these mice should be highly susceptible to bacterial infection, the researchers made the unexpected and counterintuitive discovery that NF- $\kappa$ B-deficient mice were able to clear bacteria that cause a skin infection even more quickly than normal mice.

"We discovered that loss of NF- $\kappa$ B caused mice to produce a potent immune-activating molecule known as interleukin-1 beta (IL-1 $\beta$ ), which in turn stimulated their bone marrow to produce dramatically increased numbers of white blood cells known as neutrophils," said Karin. Neutrophils are the body's front-line defenders against infection, capable of swallowing and killing bacteria with a variety of natural antibiotic enzymes and proteases.

The new research demonstrates that the innate immune system deploys two effective strategies to deal with invasive bacterial infection, and that the IL-1 $\beta$  system provides an important safety net when NF- $\kappa$ B falls short.

"Having a backup system in place is critical given the diverse strategies that bacterial pathogens have evolved to avoid bacterial clearance," said Victor Nizet, MD, professor of pediatrics and pharmacy, whose laboratory conducted the infectious challenge experiments in the study. "A number of bacteria are known to suppress pathways required for NF- $\kappa$ B activation, so IL-1 $\beta$  signaling could help us recognize and respond to these threats."

While helpful in short-term defense against a severe bacterial infection, the dramatic increase in neutrophil counts seen in the NF- $\kappa$ B-deficient mice ultimately came at a cost. Over many weeks, these activated immune cells produced inflammation in multiple organs and led to the premature death of the animals. Long-term blockade of NF- $\kappa$ B signaling has been explored extensively by the biotechnology and pharmaceutical industry as a strategy for anti-inflammatory or anti-cancer therapy, perhaps unaware of the risks suggested by this new research.

"One might contemplate adding a second inhibitor of IL-1 $\beta$  signaling to protect against the over-exuberant neutrophil response," said Karin. "Unfortunately, loss of both the NF- $\kappa$ B pathway and the backup IL-1 $\beta$  pathway rendered the mice highly susceptible to invasive bacterial infection which they no longer cleared."

Altogether, the UC San Diego research sheds new light on the complex and elegant regulatory pathways required for a highly effective innate immune system. The scientists noted that future investigations must take into account these interrelationships in order to design novel drugs against inflammatory diseases that achieve their treatment goals while minimizing the risk of infection.

*Lead authors of the study were former UC San Diego postdoctoral fellows Li-Chung Hsu, now at National Taiwan University in Taipei, and Thomas Enzler, currently at the University of Göttingen in Germany. Additional contributors include Guan-Yi Yu and Vladislav Temkin of the UCSD Department of Pharmacology; Anjuli Timmer of the UCSD Department of Pediatrics; Jun Seita and Irving Weissman of the Institute for Stem Cell Biology at Stanford University School of Medicine; Chih-Yuan Lee, Ting-Yu Lai, Guann-Yi Yu, and Liang-Chuan Lai of National Taiwan University; and Ursula Sinzig and Thiha Aung of the University of Goettingen.*

*The research of Karin, Nizet and Weissman was supported by grants from the National Institutes of Health.*

<http://news.discovery.com/earth/life-began-3-billion-years-ago-dna-101220.html>

## **Life on Earth Began Three Billion Years Ago**

***A mathematical model dates back the evolution of genes critical to life to three billion years ago.***

Life on Earth dramatically surged around three billion years ago, possibly when primitive forms developed more efficient ways to harness energy from sunlight, according to a study published on Sunday in *Nature*.

The conclusion is made by scientists at the Massachusetts Institute of Technology (MIT), who built a "genomic fossil," in essence a mathematical model that took 1,000 key genes that exist today and calculated how they evolved from the very distant past.

The collective genome of all life expanded massively between 3.3 and 2.8 billion years ago, and during this time 27 percent of all presently existing gene families came into being, the study suggests.

Investigators Eric Alm and Lawrence David said the great surge probably came through the advent of a biochemical process called modern electron transport. This is a key biological function, involving the movement of electrons within the membranes of cells. It is central to plants and to some microbes, enabling them to harvest energy from the sun through photosynthesis and to breathe oxygen.

The big change, which Alm and David dub the Archean expansion, was followed some 500 million years later by a phenomenon known as the Great Oxidation Event, when Earth's atmosphere became progressively flooded with oxygen. The Great Oxidation Event is possibly the biggest species turnover in Earth's history, as primitive or microbial lifeforms that were non-oxygen breathers died out and were replaced by bigger, smarter aerobic forms.

"Our results can't say if the development of electron transport directly caused the Archean Expansion," David admitted. "Nonetheless, we can speculate that having access to a much larger energy budget enabled the biosphere to host larger and more complex microbial ecosystems."

Early fossils date back to a period called the Cambrian Explosion, some 588 million years ago. But pre-Cambrian lifeforms were soft-bodied and, with rare exceptions, did not leave a fossil imprint. Even so, they did leave a legacy in abundant DNA, which explains the bid to recreate the "genomic fossil" by computer.

"What is really remarkable about these findings is that they prove that the histories of very ancient events are recorded in the shared DNA of living organisms," said Alm.

"Now that we are beginning to understand how to decode that history, I have hope that we can reconstruct some of the earliest events in the evolution of life in great detail."

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### **Component in common dairy foods may cut diabetes risk**

**Boston, MA – Scientists at the Harvard School of Public Health (HSPH) and collaborators from other institutions have identified a natural substance in dairy fat that may substantially reduce the risk of type 2 diabetes.**

The compound, trans-palmitoleic acid, is a fatty acid found in milk, cheese, yogurt, and butter. It is not produced by the body and so only comes from the diet.

Reporting in the December 21, 2010, issue of *Annals of Internal Medicine*, investigators led by Dariush Mozaffarian, associate professor in the Department of Epidemiology at HSPH and Division of Cardiovascular Medicine, Brigham and Women's Hospital and Harvard Medical School, and Gökhan S. Hotamisligil, J.S. Simmons Professor of Genetics and Metabolism and chair of the Department of Genetics and Complex Diseases at HSPH, explain that trans-palmitoleic acid may underlie epidemiological evidence in recent years that diets rich in dairy foods are linked to lower risk of type 2 diabetes and related metabolic abnormalities. Health experts generally advise reducing full-fat dairy products, but trans-palmitoleic acid is found in dairy fat.

The HSPH researchers examined 3,736 participants in the National Heart, Lung, and Blood Institute-funded Cardiovascular Health Study, who have been followed for 20 years in an observational study to evaluate risk factors for cardiovascular diseases in older adults. Metabolic risk factors such as blood glucose and insulin levels, and also levels of circulating blood fatty acids, including trans-palmitoleic acid, were measured using stored blood samples in 1992, and participants were followed for development of type 2 diabetes.

At baseline, higher circulating levels of trans-palmitoleic acid were associated with healthier levels of blood cholesterol, inflammatory markers, insulin levels, and insulin sensitivity, after adjustment for other risk factors. During follow-up, individuals with higher circulating levels of trans-palmitoleic acid had a much lower risk of developing diabetes, with about a 60% lower risk among participants in the highest quintile (fifth) of trans-palmitoleic acid levels, compared to individuals in the lowest quintile.

"This type of observational finding requires confirmation in additional observational studies and controlled trials, but the magnitude of this association is striking," said Mozaffarian, lead author of the study. "This represents an almost three-fold difference in risk of developing diabetes among individuals with the highest blood levels of this fatty acid."

In contrast to the types of industrially produced trans fats found in partially hydrogenated vegetable oils, which have been linked to higher risk of heart disease, trans-palmitoleic acid is almost exclusively found in naturally-occurring dairy and meat trans fats, which in prior studies have not been linked to higher heart disease risk.

"There has been no clear biologic explanation for the lower risk of diabetes seen with higher dairy consumption in prior studies. This is the first time that the relationship of trans-palmitoleic acid with diabetes risk has been evaluated," said Mozaffarian. "We wonder whether this naturally occurring trans fatty acid in

dairy fats may partly mimic the normal biologic role of its cis counterpart, cis-palmitoleic acid, a fatty acid that is produced in the body. In animal experiments, cis-palmitoleic acid protects against diabetes."

"Unfortunately, with modern diets, synthesis of cis-palmitoleic acid is now driven by high amounts of carbohydrate and calories in the diet, which might limit its normal protective function. We wonder whether trans-palmitoleic acid may be stepping in as a "pinch hitter" for at least some of the functions of cis-palmitoleic acid," said Mozaffarian.

Hotamisligil, the study's senior author, also emphasized the magnitude of the risk reduction. "This is an extremely strong protective effect, stronger than other things we know can be beneficial against diabetes. The next step is to move forward with an intervention trial to see if there is therapeutic value in people."

Because trans-palmitoleic acid, also known as trans-palmitoleate, is a natural compound, Hotamisligil said that conducting clinical trials should be possible. "This study represents the power of interdisciplinary work bridging basic science with population studies to realize exciting translational possibilities," he said.

*Support for the study was provided by the National Heart, Lung, and Blood Institute and National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health and the National Institutes of Health Office of Dietary Supplements and National Institute of Neurological Disorders and Stroke. A subset of additional fatty acid measurements were supported by a Searle Scholar Award.*

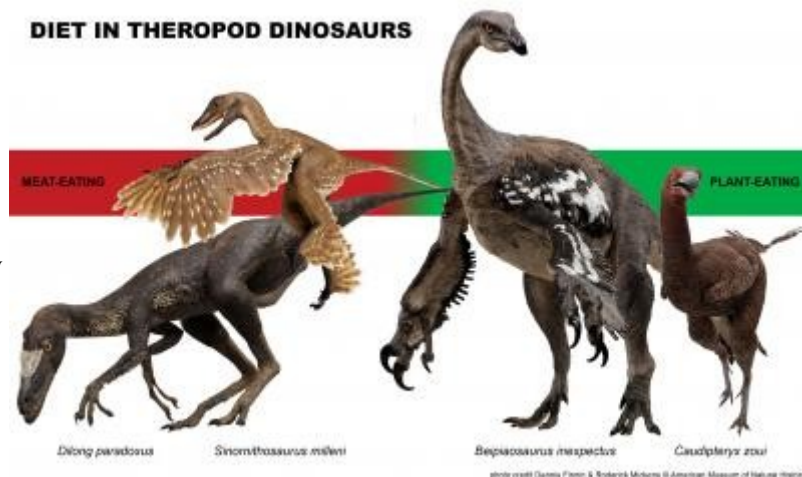
*"Trans-Palmitoleic Acid, Metabolic Risk Factors, and New-Onset Diabetes in U.S. Adults," Dariush Mozaffarian, Haiming Cao, Irena B. King, Rozenn N. Lemaitre, Xiaoling Song, David S. Siscovick, and Gökhan S. Hotamisligil, Annals of Internal Medicine, December 21, 2010*

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### **Meat-eating dinosaurs not so carnivorous after all**

#### **New research on dinosaur diet reveals that most bird-like dinosaurs were eating plants**

Tyrannosaurus rex may have been a flesh-eating terror but many of his closest relatives were more content with vegetarian fare, a new analysis by Field Museum scientists has found. The scientists, Lindsay Zanno and Peter Makovicky, who will publish their findings in the journal Proceedings of the National Academy of Sciences, used statistical analyses to determine the diet of 90 species of theropod dinosaurs. Their results challenge the conventional view that nearly all theropods hunted prey, especially those closest to the ancestors of birds. Rather, Zanno and Makovicky show that among the most bird-like dinosaurs—known as coelurosaurs—plant eating was a common way of life. "Most theropods are clearly adapted to a predatory lifestyle, but somewhere on the line to birds, predatory dinosaurs went soft," Zanno says.



***New research by Field Museum scientists finds widespread herbivory in bird-like theropod dinosaurs. Four of the 90-theropod species involved in the study shown with dietary interpretations. All four species derive from the famous feathered dinosaur beds of the Early Cretaceous Yixian Formation, P. R. China, leading the scientists to speculate that dietary diversity may have contributed to the large numbers of contemporaneous theropods in ecosystems like those of the Yixian.***

Theropods are a group of bipedal dinosaurs colloquially known as "predatory" dinosaurs. Among theropod dinosaurs, all modern birds and several groups of their closest extinct relatives belong to a subgroup known as Coelurosauria. Coelurosauria also includes the iconic hunters Tyrannosaurus and Velociraptor. Most coelurosaurs were feathered. The most intelligent dinosaurs and those with the smallest body sizes also belong to this group.

The study was funded in part by the National Science Foundation. Lead author Lindsay Zanno's research was supported by a John Caldwell-Meeker Fellowship and by a Bucksbaum Fellowship for young scientists.

#### **Pinning the Diet on the Dinosaur**

Deducing the diet of extinct animals isn't always straightforward. In all but the rarest cases, paleontologists have nothing but fossilized bones and teeth to work with. Sometimes figuring out what a dinosaur ate is fairly obvious. No one doubts, for example, that the bone-crunching teeth and jaws of Tyrannosaurus rex were the tools of a megapredator or that the tooth batteries of Triceratops were used for shearing plant material. However, many coelurosaurian dinosaurs have more ambiguous adaptations such as peg-like teeth at the front of the mouth or no teeth at all so determining their diet has been a challenge. "These oddball dinosaurs have

been the subject of much speculation" says Makovicky, "but until now, we have not had a reliable way to choose between competing theories as to what they ate."

Fortunately a small percentage of these species also preserve clear-cut evidence of diet with their skeletal remains. Fossilized dinosaur dung, stomach contents, tooth marks, the presence of stones within the stomach that serve as a gastric mill for digesting vegetation, and even two dinosaur species preserved locked in the throes of combat all provide a direct window on diet. After collecting dietary data for almost 100 coelurosaur species, Zanno and Makovicky used statistical analyses to test whether certain skeletal traits (such as the loss of teeth or a long neck) could be found to correlate with direct evidence of plant eating among coelurosaurian dinosaurs.

They found almost two dozen anatomical features statistically linked to direct evidence of herbivory including a toothless beak. "Once we linked certain adaptations with direct evidence of diet, we looked to see which other theropod species had the same traits," Zanno said, "then we could say who was likely a plant eater and who was not."

Applying their data on diet, the researchers found that 44 theropod species distributed across six major lineages were eating plants and that the ancestor to most feathered dinosaurs and modern birds had probably already lost its appetite for flesh alone. Because plant eating was found to be so widespread in Coelurosauria, the hypercarnivorous habits of *T. rex* and other meat eating coelurosaurs like *Velociraptor* should be viewed "more as the exception than the rule," Zanno says. "This new research firmly supports what we've have been speculating about for some time," she says. "Its time to start seeing these animals in a new evolutionary context." The researcher's findings also suggest that iconic predators such as the *Velociraptor* of Jurassic Park fame and their close relatives may have evolved from omnivorous ancestors—an idea Zanno proposed last year in 2009 based on the discovery of a new plant-eating coelurosaur, *Nothronychus graffami*.

### **How to Make a Plant Eating "Predator"**

Besides identifying diet, the researchers analyzed whether different groups of coelurosaurs followed the same evolutionary pathways toward an herbivorous diet. They found that over time, species lost their flesh-rendering teeth, developing strange tooth types such as peg-, wedge-, and leaf-shaped teeth, and ultimately, some lost most or all of their teeth altogether and replaced them with a bird-like beak. While the new research suggests that dinosaurs evolved beaks to aid their transition to plant eating, once that innovation was accomplished, beaks continued evolving into a myriad of forms and help support a high degree of dietary diversity in modern birds. "This is a clear-cut indication that the repeated evolution of a toothless beak in theropod dinosaurs is linked to plant eating," Zanno says. However, "once a beak appeared on the scene, it continued to evolve. Theropods would have used their beaks in a myriad of ways; they still do," she said.

Zanno and Makovicky also found that a toothless beak only evolved in lineages known to have had a gastric mill for grinding plants. In lineages where a gastric mill is not yet known, such as the bizarre, sickle-clawed therizinosaur, the species retain teeth at the back of the mouth for shredding plant material. Besides losing teeth and evolving beaks, the researchers found that as several lineages of coelurosaur turned to plant eating, they also evolved longer necks, which may have helped the animals to expand their browsing range.

### **A Dietary Advantage?**

Coelurosaurian theropods were an extremely successful group of dinosaurs throughout the Cretaceous Period (145-65 million years ago) and many different species of coelurosaurs inhabited the same ancient environments but scientists have yet to figure out why. One theory is that the break up of continents and origin of new habitat opened up new dietary niches for coelurosaurs to explore. Zanno and Makovicky speculate that dietary diversification also may have played a role in their success. "The ability to eat plant materials may have played a pivotal role in allowing coelurosaurian dinosaurs to achieve such remarkable species diversity," Zanno noted, "but more study is needed to understand what role dietary shifts may play in evolutionary processes."

Because coelurosaurian dinosaurs include the closest extinct relatives of birds, understanding their biology is also extremely important to understanding how, why, and under what conditions birds evolved and first took flight.

"We don't know what drove the ancestors to birds to take flight," she says, "seeking food in the trees is just one of many possibilities."

Using statistical analysis to find correlations between physical traits and diet could offer a new window as to how evolution works, the researchers said, and these techniques could be used to provide new insight into the common practice of becoming an herbivore throughout vertebrate history. Makovicky summarizes, "Being able to establish diet in extinct animals with confidence will allow us to start tackling even broader questions, such as whether animals tend to increase in body and diversity when they evolve herbivory."

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## **New research shows virus previously linked to chronic fatigue syndrome is a lab contaminant**

***A virus previously thought to be associated with chronic fatigue syndrome is not the cause of the disease, a detailed study has shown. The research shows that cell samples used in previous research were contaminated with the virus identified as XMRV and that XMRV is present in the mouse genome.***

XMRV was first linked to chronic fatigue syndrome – also known as myalgic encephalomyelitis (ME) – in a study published in October 2009, where blood samples from chronic fatigue syndrome patients were found to have traces of the virus. XMRV had also been identified previously in samples from certain prostate cancer patients. The new study, published in *Retrovirology*, identifies the source of XMRV in chronic fatigue syndrome samples as being cells or mouse DNA rather than infection by XMRV. The research does not rule out a virus cause of chronic fatigue syndrome - it is simply not this virus.

The research team developed improved methods to detect XMRV against the genetic noise of other sequences and make recommendations for future study of virus causes of human disease.

"Our conclusion is quite simple: XMRV is not the cause of chronic fatigue syndrome," says Professor Greg Towers, a Wellcome Trust Senior Research Fellow at University College London (UCL). "All our evidence shows that the sequences from the virus genome in cell culture have contaminated human chronic fatigue syndrome and prostate cancer samples. "It is vital to understand that we are not saying chronic fatigue syndrome does not have a virus cause – we cannot answer that yet – but we know it is not this virus causing it."

The team, from University College London, Wellcome Trust Sanger Institute and University of Oxford, showed clearly that the experimental design of previous studies would pick up sequences that resembled XMRV; however, in this improved study, they could prove that the signal was from contamination by a laboratory cell line or mouse DNA. The sequences from the contaminated cell line and chronic fatigue patient samples were extremely similar, contrary to the pattern of evolution expected during the infectious spread of a virus in a human population.

They also showed that the existing methods would indicate that one in fifty human cell lines they examined were infected with XMRV-related viruses: they showed that contamination of human tumour cells with XMRV-related viruses is common and that a principal prostate cancer line used is contaminated.

"When we compare viral genomes, we see signs of their history, of how far they have travelled in space or time," says Dr Stéphane Hué, Post Doctoral Researcher at UCL.

"We would expect the samples from patients from around the world, collected at different times, to be more diverse than the samples from within a cell line in a lab, where they are grown under standard conditions. During infection and transmission in people, our immune system would push XMRV into new genetic variants. "Viral infection is a battle between the virus and the host and XMRV does not have the scars of a virus that transmits between people."

Together the results demonstrate that XMRV does not cause chronic fatigue syndrome or prostate cancer in these cases. The team's methods suggest ways to ensure that virus contamination does not confound the search for a cause of disease in future work.

The authors propose that more rigorous methods are used to prevent contamination of cell and DNA samples. They also suggest that consistent and considered standards are needed for identifying viruses and other organisms as cause of a disease.

"Increasingly, we are using DNA-based methods to accelerate our understanding of the role of pathogens in disease," explains Professor Paul Kellam, Virus Genomics group leader from the Wellcome Trust Sanger Institute. "These will drive our understanding of infection, but we must ensure that we close the circle from identification to association and then causation. The strongest lesson is that we must fully use robust guidelines and discriminatory methods to ascribe a cause to a disease."

*The research paper can be found online at <http://www.retrovirology.com/content/7/1/111>.*

[http://www.eurekalert.org/pub\\_releases/2010-12/hu-yfc122010.php](http://www.eurekalert.org/pub_releases/2010-12/hu-yfc122010.php)

## **Young female chimpanzees appear to treat sticks as dolls**

***Finding adds to growing evidence of a biological basis for gender-specific play in humans***

CAMBRIDGE, Mass. -- The must-have gift for young female chimpanzees this holiday season might be in the Christmas tree, not under it.

That's the finding of scientists at Harvard University and Bates College, who say female chimpanzees appear to treat sticks as dolls, carrying them around until they have offspring of their own. Young males engage in such behavior much less frequently.

The new work by Sonya M. Kahlenberg and Richard W. Wrangham, described this week in the journal *Current Biology*, provides the first suggestive evidence of a wild non-human species playing with rudimentary dolls, as well as the first known sex difference in a wild animal's choice of playthings.

The two researchers say their work adds to a growing body of evidence that human children are probably born with their own ideas of how they want to behave, rather than simply mirroring other girls who play with dolls and boys who play with trucks. Doll play among humans could have its origins in object-carrying by earlier apes, they say, suggesting that toy selection is probably not due entirely to socialization.

"In humans, there are robust sex differences in children's toy play, and these are remarkably similar across cultures," says Kahlenberg, a lecturer in biology at Bates who conducted the research as a postdoctoral researcher in Wrangham's group at Harvard. "While socialization by elders and peers has been the primary explanation, our work suggests that biology may also have an important role to play in activity preferences."

In 14 years of data on chimpanzee behavior at the Kibale National Park in Uganda, Kahlenberg and Wrangham counted more than 100 examples of stick-carrying. In many cases young females weren't using the sticks for foraging or fighting, as adults sometimes do, or for any other discernable purpose.

Some young chimpanzees carried sticks into the nest to sleep with them and on one occasion built a separate nest for the stick. The researchers even witnessed the animals playing a version of the "airplane game," lying on their backs with their "offspring" balanced across their upraised hands.

"We have seen juveniles occasionally carrying sticks for many years, and because they sometimes treated them rather like dolls, we wanted to know if in general this behavior tended to represent something like playing with dolls," says Wrangham, the Ruth Moore Professor of Biological Anthropology at Harvard. "If the doll hypothesis was right we thought that females should carry sticks more than males do, and that the chimpanzees should stop carrying sticks when they had their first offspring. We have now watched enough young chimpanzees to test both points."

Kahlenberg and Wrangham's observations included a few adult females carrying sticks, but only before they became mothers for the first time. Their finding clearly links juvenile play to adult behavior, since female chimpanzees, not males, carry infants more than 99 percent of the time.

"Obviously in humans there is a huge role for peers, parents, and others to influence a child's preferences for different kinds of toys, and the same may well be true of chimpanzees," Wrangham says. "One of the things that makes our finding fascinating is that there is little evidence of anything comparable in other chimpanzee communities, which raises the possibility that the chimpanzees are copying a local behavioral tradition. So this may be a lovely case of biological and social influences being intertwined."

*Kahlenberg and Wrangham's research was supported by the National Science Foundation, the Leakey Foundation, the National Geographic Society, the Getty Foundation, and the Wenner-Gren Foundation.*

[http://www.eurekalert.org/pub\\_releases/2010-12/smu-rwd122010.php](http://www.eurekalert.org/pub_releases/2010-12/smu-rwd122010.php)

## **Rodents were diverse and abundant in prehistoric Africa when our human ancestors evolved**

### **Analysis documents more than 130 formally named genera, which can help shed light on human evolution**

Rodents get a bad rap as vermin and pests because they seem to thrive everywhere. They have been one of the most common mammals in Africa for the past 50 million years.

From deserts to rainforests, rodents flourished in prehistoric Africa, making them a stable and plentiful source of food, says paleontologist Alisa Winkler, an expert on rodent and rabbit fossils. Now rodent fossils are proving their usefulness to scientists as they help shed light on human evolution.

Rodents can corroborate evidence from geology and plant and animal fossils about the ancient environments of our human ancestors and other prehistoric mammals, says Winkler, a research professor at Southern Methodist University and an assistant professor at the University of Texas Southwestern Medical Center, both in Dallas.

*This jaw of a 20 million-year-old cane rat was discovered by scientists at a hominoid locality in northern Uganda. The specimen is at the Uganda National Museum in Kampala. Dale Winkler, SMU*



"Rodents are often known in abundance, and there are many different kinds from a number of famous hominid and hominoid localities," says Winkler. "Many paleoanthropologists are very interested in the faunal and ecological context in which our own species evolved."

## **Rodents: World's most abundant mammal — and Africa's too**

Rodents — rats, mice, squirrels, porcupines, gerbils and others — are the largest order of living mammals, constituting 42 percent of the total mammalian diversity worldwide. That's according to data drawn from the research literature in an analysis by Winkler and her colleagues, paleontologists Christiane Denys of the Museum National d'Histoire Naturelle in Paris and D. Margaret Avery of the Iziko South African Museum in Cape Town.

Their review documents more than 130 formally named genera in "Fossil Rodents of Africa," the first comprehensive summary and distribution analysis of Africa's fossil rodents since 1978. To see a flickr slideshow of rodent fossil images, go to [http://blog.smu.edu/research/2010/12/rodents\\_were\\_diverse\\_and\\_abund.html](http://blog.smu.edu/research/2010/12/rodents_were_diverse_and_abund.html) or to flickr, <http://www.flickr.com/photos/52146845@N06/5269535741/>.

The analysis is a chapter in the new 1008-page scientific reference book "Cenozoic Mammals of Africa" (University of California Press, 2010), the first comprehensive scientific review of Africa's fossil mammals in more than three decades. The book comprises 48 chapters by 64 experts, summarizing and interpreting the published fossil research to date of Africa's mammals, tectonics, geography, climate and flora of the past 65 million years.

### **Rodents are human's best friend?**

Rodents have been around much longer than humans or human ancestors in Africa, with the earliest from northern Africa dating from about 50 million years ago. Today scientists are aware of 14 families of rodents in Africa.

Winkler cites locales where fossils of the sharp-toothed, gnawing creatures have been found relevant to our human ancestors:

- \* Ethiopia's Middle Awash, where some fossils date to when the chimpanzee and human lines split 4 million to 7 million years ago and where the famous "Ardi" primate was discovered;
- \* Tanzania's Olduvai Gorge, dubbed the "Cradle of Mankind";
- \* The Tugen Hills and Lake Turkana sites of Kenya, where important human ancestor fossils have been discovered;
- \* In younger southern African cave faunas dating to the Stone Age.

Their fossils also have been found in other older Eastern Africa sites, where apes and humans have been linked to the monkey lineage.

"At many of these sites, identification of Africa's rodents provides important collaborating information on the ecology of the locales and on environmental change through time," the authors write.

Rodent diversity likely underestimated; more fossils than scientists

The diversity of ancient Africa's rodents most likely has been underestimated, say the authors. Just how much isn't known, though, because the quantity of rodent fossils being discovered far exceeds the handful of scientists who specialize in identifying and studying the specimens.

That diversity continues to expand. The last exhaustive analysis of Africa's rodents was carried out by R. Lavocat in 1978. At that time scientists recorded 54 genera, 76 fewer than those documented by Winkler, Denys and Avery in their analysis.

Winkler and her colleagues summarize the distribution and ecology of existing rodent families, as well as the systematics, biochronology and paleobiogeography of rodent families in Africa's fossil record. The diversity they document reflects "the wide variety of habitats present on the continent" and paints a picture of Africa's paleoecology.

Given the huge rodent diversity in modern Africa, "it is likely that such an extensive fauna was also present in the past," the scientists write.

Tremendous diversity reflects wide variety of habitats

An example of that relationship is the scaly-tailed flying squirrel, an exclusively African group of forest-dwelling rodents that are not related to true squirrels. They are well known from about 18 million to 20 million years ago in eastern Africa, Winkler says, suggesting the presence of closed habitats, such as forests. That corroborates other evidence of forests from fossil animals, plants and geology, she says.

"Although there are even older scaly-tailed flying squirrels known from the currently arid regions of northern Africa," says Winkler, "they do not appear to have been gliders, as are most current forms, and the question of when members of the group first developed gliding locomotion still remains."

*Funding for "Cenozoic Mammals of Africa" came from the Swedish Research Council; the University of Michigan's College of Literature, Science, and the Arts, and Museum of Paleontology; and the Regents of the University of California.*

## **Age plays too big a role in prostate cancer treatment decisions**

**Older men with high-risk prostate cancer frequently are offered fewer – and less effective – choices of treatment than younger men, potentially resulting in earlier deaths, according to a new UCSF study.**

The scientists found that men above age 75 with high-risk prostate cancer often are under-treated through hormone therapy or watchful waiting alone in lieu of more aggressive treatments such as surgery and radiation therapies. Instead, say the researchers, old age should not be viewed as a barrier to treatments that could lead to potential cures.

"There is a disconnect between risk and treatment decisions among older men," said senior investigator Matthew R. Cooperberg, MD, MPH. "Patient age is strongly influencing treatment decisions, so we sought to understand whether age plays a role in risk of the disease and survival. We found that under-treatment of older men with high-risk disease might in part explain higher rates of cancer mortality in this group. There is also pervasive over-treatment of low-risk disease in this age group. Overall, treatment needs to be selected more based on disease risk and less based on chronologic age."

The study is published by the "Journal of Clinical Oncology," and is available online at

<http://jco.ascopubs.org/content/early/2010/12/02/JCO.2010.30.2075.full.pdf+html?sid=fe9ef2e4-1379-4e7b-ab6c-c33796334de4>

Prostate cancer is the most common form of cancer in men and the second most common cause of cancer death after lung cancer. This year, an estimated 217,730 men will be diagnosed with the disease, and 32,050 men will die from it, reports the American Cancer Society. Moreover, prostate cancer is the most common malignancy among older men: 64 percent of new cases in the United States this year were diagnosed in men older than 65, and 23 percent in men above 75.

Yet most studies delving into optimal treatment options focus on men younger than 75. The new UCSF study is among the first to explore the relationship between age, disease risk and survival among prostate cancer patients.

The researchers studied men in the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) database, a longitudinal, observational disease registry of men with prostate cancer who were recruited from urology practices throughout the United States. At the time of the study, the database contained information on 13,805 patients.

The scientists found that older patients are more likely to have high-risk prostate cancer at the point of diagnosis, and less likely to receive potentially curative local therapy. Yet when older, high-risk men received more aggressive treatment, they had a 46 percent lower death rate compared with patients treated more conservatively with hormonal therapy or watchful waiting. The finding, the researchers say, suggests that underuse of aggressive therapy may in part explain the higher death rates of older men with the disease.

"Age does not independently predict prostate cancer survival," said Peter R. Carroll, MD, MPH, chair of the UCSF Department of Urology and co-leader of the prostate program at the UCSF Helen Diller Family Comprehensive Cancer Center. He is a co-author of the paper. "Our findings support making treatment decisions on the basis of disease risk and life expectancy rather than on chronologic age."

The researchers note that the U.S. Preventive Services Task Force specifically recommends against screening men age 75 or older, but that position is based on studies on younger men, and furthermore does not account for health status or other diseases that the patients may have which would affect life expectancy.

"Older men with high-risk disease frequently die of prostate cancer and under-treatment might be a factor in their deaths," said Cooperberg, a prostate cancer specialist in the UCSF Department of Urology and the Helen Diller cancer center. "The notion of age as a primary determinant should be reconsidered. Patients with aggressive local disease should be offered a chance of aggressive therapy that might cure them regardless of their age."

Traditionally, Cooperberg said, physicians have feared the risks of surgery on their older patients. But for older patients with localized, high-risk disease – and a life expectancy of more than 10 years – the researchers recommend that surgical treatment and radiation be considered.

"Surgery and radiation risks do go up with age, but it may be that we are focusing too much on risk than on benefit," said Cooperberg. "We need a better balance between risk and benefit."

*Seth K. Bechis, a UCSF medical student now in residency at Massachusetts General Hospital, is the lead author of the paper. Carroll and Cooperberg report receiving honoraria unrelated to the study from Takeda Pharmaceuticals, and Cooperberg additionally from Abbott Laboratories. Abbott supports CaPSURE in part, and additional funding is provided through several federal grants.*



## Seeing double: Africa's 2 elephant species

**Contrary to the belief of many scientists (as well as many members of the public), new research confirms that Africa has two—not one—species of elephant.**

Scientists from Harvard Medical School, the University of Illinois, and the University of York in the United Kingdom used genetic analysis to prove that the African savanna elephant and the smaller African forest elephant have been largely separated for several million years.

The researchers, whose findings appear online in PLoS Biology, compared the DNA of modern elephants from Africa and Asia to DNA that they extracted from two extinct species: the woolly mammoth and the mastodon. Not only is this the first time that anyone has generated sequences for the mastodon nuclear genome, but it is also the first time that the Asian elephant, African forest elephant, African savanna elephant, the extinct woolly mammoth, and the extinct American mastodon have been looked at together.

"Experimentally, we had a major challenge to extract DNA sequences from two fossils—mammoth and mastodons—and line them up with DNA from modern elephants over hundreds of sections of the genome," says research scientist Nadin Rohland of the Department of Genetics at Harvard Medical School.

According to David Reich, associate professor in the same department, "The surprising finding is that forest and savanna elephants from Africa—which some have argued are the same species—are as distinct from each other as Asian elephants and mammoths."

Researchers only had DNA from a single elephant in each species, but had collected enough data from each genome to traverse millions of years of evolution to the time when elephants first diverged from each other.

"The divergence of the two species took place around the time of the divergence of the Asian elephant and woolly mammoths," says Professor Michi Hofreiter, who specializes in the study of ancient DNA in the Department of Biology at York. "The split between African savanna and forest elephants is almost as old as the split between humans and chimpanzees. This result amazed us all."

The possibility that the two might be separate species was first raised in 2001, but this is the most compelling scientific evidence so far that they are indeed distinct.

Previously, many naturalists believed that African savanna elephants and African forest elephants were two populations of the same species, despite the significant size differences. The savanna elephant has an average shoulder height of 3.5 meters whereas the forest elephant has an average shoulder height of 2.5 meters. The savanna elephant weighs between six and seven tons, roughly double the weight of the forest elephant.

DNA analysis revealed a wide range of genetic diversity within each species. The savanna elephant and woolly mammoth have very low genetic diversity, Asian elephants have medium diversity, and forest elephants have very high diversity. Researchers believe that this is due to varying levels of reproductive competition among males.

"We now have to treat the forest and savanna elephants as two different units for conservation purposes," says Alfred Roca, assistant professor in the Department of Animal Sciences at the University of Illinois. "Since 1950, all African elephants have been conserved as one species. Now that we know the forest and savanna elephants are two very distinctive animals, the forest elephant should become a bigger priority for conservation purposes."

*This research was funded by the Max Planck Society and by a Burroughs Wellcome Career Development Award in Biomedical Science.*

<http://www.bbc.co.uk/news/health-12048275>

## 'Chocolate cough remedy' in sight

**A chemical in cocoa could soon be turned into a medicine for persistent cough, researchers claim.**

Scientists are carrying out the final stages of clinical trials of a drug that contains theobromine, an ingredient found in chocolate and cocoa. The UK developers say the drug could be on the market within two years.

Every year in Britain an estimated 7.5m people suffer from persistent cough - a cough lasting more than two weeks. Most current medicines used to control the symptoms are opiate-based ones like cough syrups containing codeine, a narcotic. But in October the Medicines and Health products Regulatory Agency (MHRA) said under-18s should not take codeine-based remedies, because the risks outweighed the benefits.

### Active ingredient

Researchers say the new theobromine treatment should not have this problem. And being flavourless, it can be taken by those who dislike chocolate. Theobromine is thought to work by inhibiting the inappropriate firing of the vagus nerve, which is a key feature of persistent cough. The final stage of the drug's testing is set to begin in the next few months. The drug, called BC1036, is being developed by the private UK company SEEK.

Manfred Scheske, CEO of Consumer Health at SEEK said: "I am very excited to announce the progression for the late-stage development of BC1036, which has the potential to dramatically impact the treatment of persistent cough and could greatly benefit the quality of life of persistent cough sufferers."

Professor Alyn Morice of the Hull Cough Clinic said there was a need for new treatments.

"Thousands of people across the UK suffer from persistent cough, and due to the drawbacks of current opioid drugs such as codeine, we are in desperate need of a non-opioid treatment with a drastically improved side effect profile for patients."

[http://news.bbc.co.uk/earth/hi/earth\\_news/newsid\\_9290000/9290068.stm](http://news.bbc.co.uk/earth/hi/earth_news/newsid_9290000/9290068.stm)

### **Dust mites 'swarm' around houses**

**By Ella Davies Earth News reporter**

#### ***Dust mites "swarm" around houses, migrating as a group in search of moisture, according to a new study.***

The collective movement happens when mites leave a dry area in search of higher humidity - the greatest source of which in a house is its human occupants. Mites gain nutrients from dead skin but also depend on moist air for survival. Millions of dust mites are found in the average home and their droppings are known to trigger asthma attacks.

In findings published in the journal *Ethology*, scientists reveal the previously unknown sociable side of house dust mites (*Dermatophagoides pteronyssinus*).

"We expected the mites to move to areas of higher humidity, because they are dependent on air moisture to survive," said co-author Anne-Catherine Mailleux. "However, the fact that they attract each other and prefer to move together rather than independently from one another was an important finding."

Researchers knew that house dust mites were unable to drink and depended on moisture in the air to survive.

During their study they observed that male adult mites and nymphs moved as a group from a dry area in search of higher humidity. When offered the choice of more than one path providing access to moister air, mites were able to perceive which branch previous mites had chosen. More often than not, they then followed these other mites.

The study showed that, by tending to choose the same routes, dust mites travel collectively or "swarm".

Although usually associated with flying insects, swarming is defined as the collective movement of a large number of organisms. This behaviour has been observed in a variety of species but was unknown in dust mites.

"So far, mites had not been considered as "social" animals, and this is the first study that shows that they tend to stick together when on the move," explained Ms Mailleux. "This suggests that they need each other for some reason, that they are better in a group than alone."

House dust mites are barely visible to the human eye, measuring less than half a millimetre long. Millions can be found in the average home in Europe, Asia and the US. Due to their need for moist air, they are most often found in bedding such as pillows and duvets. Their droppings are a known trigger for attacks amongst asthma sufferers. In allergic individuals the human immune system can identify mite droppings as a threat and creates antibodies to fight it, causing irritation to the airways.

The behaviour of house dust mites is therefore of considerable interest to those studying allergies.

"Knowing how mites behave can be very helpful when taking measures to prevent their populations from growing," says Ms Mailleux.

<http://www.newscientist.com/article/dn19895-thinnest-ever-camera-sees-like-a-trilobite.html>

### **Thinnest ever camera sees like a trilobite**

**\* 11:42 21 December 2010 by Kate McAlpine**

#### ***An unusual arthropod eye design that maximises image resolution has inspired the design of the thinnest stills and video camera yet made.***

At just 1.4 millimetres thick, the camera could replace those used in mobile phones, where space carries a hefty premium. It produces 0.38 megapixel images and has a wider field of view than the standard cameras on many phones.

The compound eyes of most arthropods contain thousands of tiny lenses, each of which resolves light to a point on a photoreceptor behind. But some trilobites, an extinct class of arthropods common in the Palaeozoic era, had an unusually small number of relatively large lenses. Each lens pointed in a different direction, and

#### **DUST MITE FACTS**

*House dust mites are acari, a subclass of arachnids and have eight legs*  
*At less than half a millimetre in length, they are barely visible to the naked eye*  
*The human immune system can "recognise" the mites and produce antibodies in response. This can trigger an allergic reaction*

each resolved a full image on the retina rather than contributing a single point of light to the final image. This boosted the total resolution of the image despite the smaller number of lenses.

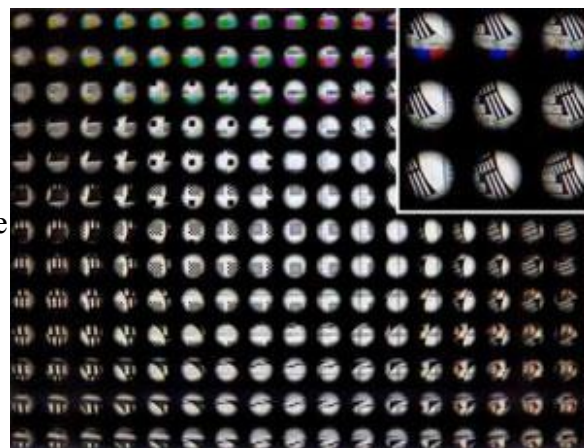
When a similar eye was discovered in an extant tiny wasp parasite in 1999, its discoverers speculated that the arrangement helps to deliver the largest, brightest image possible on such a miniscule head.

### Trilobite camera

Andreas Brückner of the Fraunhofer Institute of Applied Optics and Precision Engineering in Jena, Germany, wondered whether designing a camera to work in the same way could likewise provide high-resolution, clear images in a tiny device.

Along with his colleagues, he designed an electronic cluster eye that can take 221 miniature images – each 39 pixels to a side which are then stitched together into a single image of 700 by 550 pixels.

This is not the first compound-eye-inspired camera to be created. Earlier designs involved taking several hundred low-resolution images of the same scene, and using a "super-resolution technique" to create a final, higher resolution image.



*Just like a trilobite? (Image:Brückner /Optics Express)*

Brückner's design is potentially more useful as stitching images together is a less computationally intense process than applying a super-resolution technique, and so the camera can process images rapidly enough to take video sequences. "It should be feasible to run the processing in real time on a smart phone," says Brückner. So far, the team have managed to record video at 13 frames per second, but say that simple modifications should speed it up to 30 frames per second.

### Secondary eye

Jun Tanida, who is developing another compound-eye camera at the University of Osaka in Japan, is impressed that the team has marked out a path for industrial production and believes that the camera could appear in devices in five years.

In addition to everyday electronics, Brückner would like to see these used in medicine, or on the gripper hands of robots as a secondary eye, providing a view as the hand closes in on an object and blocks the main camera. The group is already at work on their next models. These include one of equal resolution but under 1 millimetre thick, and one 1.5 millimetres thick with 1 megapixel resolution.

*Journal reference: Optics Express, DOI: 10.1364/OE.18.024379*

[http://www.eurekalert.org/pub\\_releases/2010-12/mc-rfg122210.php](http://www.eurekalert.org/pub_releases/2010-12/mc-rfg122210.php)

### Researchers find gene that protects against dementia in high-risk individuals

**JACKSONVILLE, Fla. — Neuroscientists had assumed that a mutation in the progranulin gene, which makes the progranulin protein and supports brain neurons, was sufficient to produce a kind of dementia known as frontotemporal lobar degeneration (FTLD). But now an international team of scientists led by researchers at Mayo Clinic's campus in Florida have found another genetic factor they say appears to protect against the disorder in progranulin mutation carriers.**

In an article published in the Dec. 22, 2010, issue of *Neurology*, the medical journal of the American Academy of Neurology, the researchers report that people with a mutated progranulin gene who also inherited two copies of a specific variant of the TMEM106B gene are significantly less likely to develop FTLD or they have their disease onset delayed.

"This was an unexpected but very exciting finding because it suggests that if we could understand what TMEM106B is, and how it and its variants work, this could provide a new avenue for development of an agent that protects against FTLD," says the study's lead author, neuroscientist Rosa Rademakers, Ph.D.

The study was a follow-up to a genome-wide association study led by researchers from the University of Pennsylvania School of Medicine, which included 45 centers around the world and was published in March 2010 in *Nature Genetics*. This study used postmortem brain tissue to pinpoint variation in the TMEM106B gene as a risk factor for FTLD. What these patients all had in common was that they had lesions of misfolded TDP-43 proteins inside brain neurons. Researchers found that TMEM106B variants also played a role in FTLD patients with a progranulin mutation who invariably have these brain lesions.

"This research was designed to confirm the findings of the earlier study and to expand it to see if TMEM106B could modulate progranulin levels," Dr. Rademakers says. To do this, the researchers looked for the TMEM106B variant in a new set of patients, including 82 FTLD patients who had progranulin mutations, 562 FTLD patients without mutations, as well as a group of 822 healthy controls. In the group as a whole, they

did not see a significant association with TMEM106B, but there was a very significant association between TMEM106B variants and the development of FTLD in individuals with progranulin mutations.

The researchers found that individuals with a progranulin mutation who also inherited two copies of the protective TMEM106B allele did not develop FTLD or developed it at a much later age than is typical, which is normally around age 60, Dr. Rademakers says. "Since progranulin mutation carriers produce 50 percent less progranulin protein, we believe TMEM106B may affect progranulin levels and therefore specifically works in people with progranulin mutations," she says.

In support of their hypothesis, they found that individuals carrying the protective TMEM106B allele have more progranulin in their blood plasma, suggesting that the TMEM106B allele works to increase progranulin protein levels. "The protective form of TMEM106B leads to higher levels of progranulin in the blood. Whether it also increases the levels of progranulin in the brain has not yet been studied and will be the focus of our future research," Dr. Rademakers says.

Not only could the beneficial TMEM106B allele be the basis of a novel therapy for individuals with a progranulin mutation, it might also help others who are at risk, for dementia she adds. "Subtle changes in progranulin levels have been linked to an increased risk for the development of FTLD, so now we have an interesting new lead to explore."

*The study was funded by the National Institutes of Health and the Consortium for Frontotemporal Dementia Research. The authors declare no conflicts of interest.*

[http://www.eurekalert.org/pub\\_releases/2010-12/uotm-hrb122210.php](http://www.eurekalert.org/pub_releases/2010-12/uotm-hrb122210.php)

### **High red blood cell folate levels linked to silenced tumor-suppressors** **Study examines effects of supplementation, other factors, on gene methylation**

HOUSTON — People with higher levels of folate in their red blood cells were more likely to have two tumor-suppressing genes shut down by methylation, a chemical off switch for genes, researchers report in the December issue of *Cancer Prevention Research*.

DNA hypermethylation, notes co-author Jean-Pierre Issa, M.D., professor in MD Anderson's Department of Leukemia, is found in a variety of cancers and diseases of aging, such as heart disease. Methyl groups attach to genes at sites called CpG islands and protrude like tags or book marks from the promoter region, preventing gene expression. "Our new finding is that having high levels of folate in the blood, as observed in a sensitive measure of red blood cell (RBC) folate, is related to higher levels of DNA methylation," Issa said.

Folate is a naturally occurring B-vitamin that plays a role in DNA creation, repair and function as well as red blood cell production. Pregnant women who have a folate deficiency are at elevated risk of giving birth to a child with neural tube defects, which are caused by the failure of the spinal cord or brain to fully close during development.

Folate is found in leafy vegetables, fruits, dried beans and peas. Since 1998 its synthetic version, folic acid, has been added to breads cereals, flours, pastas, rice and other grain products under order from the U.S. Food and Drug Administration. This has driven down the rate of neural tube defects in the United States, according to the U.S. Centers for Disease Control and Prevention.

Folate also is taken as a dietary supplement. The recommended daily requirement is 400 micrograms for adult men and women and an additional 400 for women capable of becoming pregnant.

Folate's effect on cancer, once thought to be mainly preventive, has become less clear in recent years, with scientists finding cancer-promoting aspects of folate intake in colorectal, prostate and other cancers.

The research team analyzed the association between folate blood levels and dietary and lifestyle factors on DNA methylation in normal colorectal tissue. They enrolled 781 patients from a parent clinical trial that compared folate to aspirin in the prevention of precancerous colorectal polyps.

They gathered demographic, lifestyle and dietary information and compared methylation of two tumor-suppressing genes between the first colonoscopy and one three years later.

The genes, ER $\alpha$  and SFRP1, are expressed in normal colorectal tissue but silenced by methylation in colon cancer. The two genes also have been found to be methylated in breast, prostate and lung tumors. Age was strongly associated with increased methylation – a finding that confirmed longstanding research. Methylation levels also varied between the rectum and right colon and among different ethnic groups for each gene.

Neither folate nor aspirin treatment were significantly associated with methylation levels. However, RBC folate was associated with methylation of both genes with significant differences emerging between the top quarter of patients with the highest RBC folate count and the bottom quarter with the lowest. RBC folate levels closely reflect long-term folate intake.

"These differences were not trivial, they were the equivalent of 10 years of extra aging for those with high RBC folate counts," Issa said. "Today it's worrisome that taking extra folate over the long term might lead to

more DNA methylation, which then might lead to extra diseases including potentially an increased chance of developing cancer and other diseases of aging," Issa said.

"The data for folate supplementation right now are very ambiguous and I personally think people taking folate should think twice about it," Issa said. "Also, these findings, added to other data, should trigger a rethinking of the U.S. position that everyone should be taking extra folate."

*This research was funded by four grants from the National Cancer Institute.*

*Co-authors with Issa are first author Kristin Wallace, Ph.D., Maria V. Grau, M.D., Jiang Gui, Ph.D., Elizabeth Barry, Ph.D., and John Baron, M.D., all of Dartmouth Medical School; A. Joan Levine, Ph.D., and Robert W. Haile, M.D., of Keck School of Medicine at the University of Southern California; Lanlan Shen, M.D., Ph.D., Randala Hamdan and Xinli Chen of MD Anderson's Department of Leukemia and Center for Epigenetics; Dennis Ahnen, M.D, University of Colorado Denver School of Medicine; and Gail McKeown-Eyssen, Ph.D., of the Dala Lana School of Public Health, University of Toronto.*

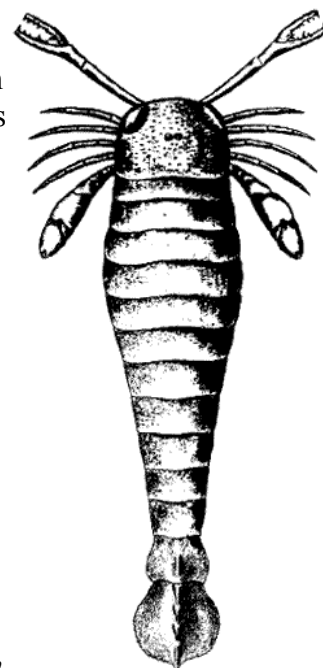
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### **Pterygotid sea scorpions: No longer terror of the ancient seas?**

**BUFFALO, NY - Experiments by a team of researchers in New York and New Jersey have generated evidence that questions the common belief that the pterygotid eurypterids ("sea scorpions") were high-level predators in the Paleozoic oceans.**

This group, which ranged the seas from about 470 to 370 million years ago (long before the dinosaurs appeared), included the largest and, arguably, scariest-looking arthropods known to have evolved on planet Earth. Reaching lengths of 2 ½ meters with a body supported by well-developed legs, and armed with a pair of forward-facing claws laden with sharp projecting spines, they seem like the Tyrannosaurus rex among the invertebrates.

But in a new study, published in volume 39 of the Bulletin of the Buffalo Society of Natural Sciences, Richard Laub (Buffalo Museum of Science) and his colleagues Victor Tollerton (Research Associate, New York State Museum) and Richard Berkof (Stevens Institute of Technology) show that the mechanical constraints on the claw of the pterygotid sea scorpion *Acutiramus* made it incapable of penetrating the external shell of a medium-sized horseshoe crab without danger of rupturing. They suggest that these imposing sea scorpions, and by extension others of their family who lived in the seas about 470 to 370 million years ago, were not necessarily the voracious predators they are commonly believed to have been. The practical operational force that could be safely applied by the claw of *Acutiramus* without causing damage to it was no more than about 5 Newtons, whereas a force of 8-17 Newtons was required to penetrate the horseshoe crab's armor.



***Pterygotus (Acutiramus) buffaloensis Pohlman late Silurian (Ludlow) New York length about 2 meters illustration from Fenton and Fenton The Fossil Book***

Laub's team also noted that the absence of an 'elbow joint' between the claws and the body of *Acutiramus* limited claw movement, making them more effective in grasping prey on the sea floor than capturing actively fleeing fish or other swimming animals. Armed with serrated spines, the claws may have been used together to both capture and shred the prey, but the predatory capabilities of *Acutiramus* would appear to lack the force necessary for this animal to operate as a major predator.

"I have long been suspicious of prevailing popular interpretations" said Dr. Roy Plotnick, Department of Earth and Environmental Sciences at the University of Illinois at Chicago, who was not involved in the study. "This is a welcome contribution that strongly supports an alternative interpretation of claw function" he said.

"Our results derail the image of these imposing-looking animals, the largest arthropods yet known to have existed, as fearsome predators, or at least as predators of other eurypterids and of the armored fishes of the time" said team leader Richard Laub, who noted that "it opens the possibility that they were scavengers or even vegetarians".

[http://www.eurekalert.org/pub\\_releases/2010-12/nsf-goe122210.php](http://www.eurekalert.org/pub_releases/2010-12/nsf-goe122210.php)

### **Genome of extinct Siberian cave-dweller linked to modern-day humans**

**Sequencing of ancient DNA reveals new hominin population that is neither Neanderthal nor modern human**

Researchers have discovered evidence of a distinct group of "archaic" humans existing outside of Africa more than 30,000 years ago at a time when Neanderthals are thought to have dominated Europe and Asia. But genetic testing shows that members of this new group were not Neanderthals, and they interbred with the ancestors of some modern humans who are alive today.

The journal Nature reported the finding this week. The National Science Foundation's Behavioral and Cognitive Sciences Division partially funded the research.

An international team of scientists led by Svante Pääbo at the Max Planck Institute of Evolutionary Anthropology in Leipzig, Germany, used a combination of genetic data and dental analysis to identify a previously unknown population of early humans, whom the researchers call "Denisovans." The name was taken from Denisova Cave in southern Siberia where archaeologists from the Russian Academy of Sciences recovered a bone in 2008.

Genetic sequencing of DNA extracted from a finger bone of a 5-10-year-old girl from the cave revealed that she was neither Neanderthal nor a modern human, but shared an ancient origin with Neanderthals. The genetic analysis also showed she had a very different history since splitting from Neanderthals, the researchers concluded. A tooth, also found in the Denisova Cave, complemented the genetic evidence. "The tooth is just amazing," said Bence Viola, a paleoanthropologist at the Max Planck Institute. "It allows us to connect the morphological and genetic information."

Analysis of the tooth revealed a shape that falls outside normal tooth variation typically seen in Neanderthals and modern humans, providing further evidence the Denisova hominins are an evolutionarily distinct group.

Another type of analysis reported by the study's authors showed Denisovans contributed 4-6 percent of their genetic material to the genomes of present-day New Guineans. "They are ancestors of people in Papua New Guinea but not of the great majority of people in Eurasia," said David Reich, a geneticist at Harvard Medical School in Boston, who led the research's population genetics analysis.

By comparing the genetic material of the Denisovans to diverse modern humans, the authors disclose a previously uncharacterized episode of gene flow between "archaic" and modern humans.

Until last year, the mainstream view in genetics was that modern humans inherited essentially their entire DNA makeup from Neanderthal-related individuals when they migrated from Africa 40,000-55,000 years ago. It was surmised they completely replaced the humans who migrated before them, including the Neanderthals whose ancestors likely made the pilgrimage hundreds of thousands of years earlier.

But sequencing and analysis of the Neanderthal genome earlier this year showed this was not the case. Neanderthals were not completely replaced, but instead contributed 1-4 percent of their genetic material to all modern non-Africans before dying out. The finding, based on Neanderthals discovered at Vindija Cave in Croatia, showed that modern humans outside of Africa are not all descended from a single out-of-Africa migration.

"We have now found evidence for a second gene flow event as well from a different source population and into a narrower set of modern human groups," said Reich. "The first gene flow event appears to have been from a population closely related to the Neanderthals, while the second gene flow event was from a population much more closely related to Denisovans."

The new research suggests rather than being an irregular occurrence, intermixing between diverged human populations may have been common. "In combination with the Neanderthal genome sequence, the Denisovan genome suggests a complex picture of genetic interactions between our ancestors and different ancient hominin groups," said Pääbo, a founder of the field of ancient DNA.

Denisovans are likely to have been widespread across a broad swath of Eurasia, since Denisovans must have existed not just in Siberia, but also thousands of miles to the south along the path of modern humans migrating out of Africa on the way to New Guinea. However, far less is known about this population archaeologically or morphologically than about the Neanderthals and modern humans who were their contemporaries in western Eurasian and in Africa.

"We hope that these results will spur archaeologists and paleontologists to study sites occupied by Denisovans," said Reich. "All we have now is a finger bone, a tooth, and a genome. However, we now know that this population existed, and new archaeological discoveries should reveal much more about their morphology and material culture." "Technically, the discovery and definition of this new population based on its DNA patterns--rather than morphology--is also fascinating," said Reich. Traditionally, hominin populations are defined based on studies of their physical form and structure. Defining them based on DNA is something made possible only by recent advances in DNA technology, and may be a harbinger for the future.

*This study also involved contributions from researchers at the Broad Institute of Harvard and Massachusetts Institute of Technology; the University of California at Santa Cruz and Berkeley; the University of Tübingen, Germany; Emory University, Georgia; the University of Montana; the University of Washington; the Institute of Evolutionary Biology, Barcelona, Spain; the Institute of Vertebrate Paleontology and Paleoanthropology of the Chinese Academy of Sciences, Beijing, China; the University of British Columbia, Vancouver, Canada; and the Institute of Archaeology & Ethnography, Russian Academy of Sciences, Siberian Branch, Novosibirsk, Russia.*

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### **Ever-sharp urchin teeth may yield tools that never need honing**

**MADISON – To survive in a tumultuous environment, sea urchins literally eat through stone, using their teeth to carve out nooks where the spiny creatures hide from predators and protect themselves from the crashing surf on the rocky shores and tide pools where they live.**

The rock-boring behavior is astonishing, scientists agree, but what is truly remarkable is that, despite constant grinding and scraping on stone, urchin teeth never, ever get dull. The secret of their ever-sharp qualities has puzzled scientists for decades, but now a new report by scientists from the University of Wisconsin-Madison and their colleagues has peeled back the toothy mystery.

Writing today (Dec. 22, 2010) in the journal *Advanced Functional Materials*, a team led by UW-Madison professor of physics Pupa Gilbert describes the self-sharpening mechanism used by the California purple sea urchin to keep a razor-sharp edge on its choppers. The urchin's self-sharpening trick, notes Gilbert, is something that could be mimicked by humans to make tools that never need honing.

"The sea urchin tooth is complicated in its design. It is one of the very few structures in nature that self-sharpen," says Gilbert, explaining that the sea urchin tooth, which is always growing, is a biomineral mosaic composed of calcite crystals with two forms – plates and fibers – arranged crosswise and cemented together with super-hard calcite nanocement. Between the crystals are layers of organic materials that are not as sturdy as the calcite crystals.

"The organic layers are the weak links in the chain," Gilbert explains. "There are breaking points at predetermined locations built into the teeth. It is a concept similar to perforated paper in the sense that the material breaks at these predetermined weak spots."

The crystalline nature of sea urchin dentition is, on the surface, different from other crystals found in nature. It lacks the obvious facets characteristic of familiar crystals, but at the very deepest levels the properties of crystals are evident in the orderly arrangement of the atoms that make up the biomineral mosaic teeth of the sea urchin.

To delve into the fundamental nature of the crystals that form sea urchin teeth, Gilbert and her colleagues used a variety of techniques from the materials scientist's toolbox. These include microscopy methods that depend on X-rays to illuminate how nanocrystals are arranged in teeth to make the sea urchins capable of grinding rock. Gilbert and her colleagues used these techniques to deduce how the crystals are organized and melded into a tough and durable biomineral.

Knowing the secret of the ever-sharp sea urchin tooth, says Gilbert, could one day have practical applications for human toolmakers. "Now that we know how it works, the knowledge could be used to develop methods to fabricate tools that could actually sharpen themselves with use," notes Gilbert. "The mechanism used by the urchin is the key. By shaping the object appropriately and using the same strategy the urchin employs, a tool with a self-sharpening edge could, in theory, be created."

*The new research was supported by grants from the U.S. Department of Energy and the National Science Foundation. In addition to Gilbert, researchers from the University of California, Berkeley; Argonne National Laboratory; the Weizmann Institute of Science; and the Lawrence Berkeley National Laboratory contributed to the report.*

[http://www.eurekalert.org/pub\\_releases/2010-12/hms-pww121710.php](http://www.eurekalert.org/pub_releases/2010-12/hms-pww121710.php)

### **Placebos work -- even without deception**

**BOSTON, Mass. - For most of us, the "placebo effect" is synonymous with the power of positive thinking; it works because you believe you're taking a real drug. But a new study rattles this assumption.**

Researchers at Harvard Medical School's Osher Research Center and Beth Israel Deaconess Medical Center (BIDMC) have found that placebos work even when administered without the seemingly requisite deception.

The study is published December 22 in *PLoS ONE*.

Placebos—or dummy pills—are typically used in clinical trials as controls for potential new medications. Even though they contain no active ingredients, patients often respond to them. In fact, data on placebos is so compelling that many American physicians (one study estimates 50 percent) secretly give placebos to unsuspecting patients.

Because such "deception" is ethically questionable, HMS associate professor of medicine Ted Kaptchuk teamed up with colleagues at BIDMC to explore whether or not the power of placebos can be harnessed honestly and respectfully.

To do this, 80 patients suffering from irritable bowel syndrome (IBS) were divided into two groups: one group, the controls, received no treatment, while the other group received a regimen of placebos—honestly described as "like sugar pills"—which they were instructed to take twice daily.

"Not only did we make it absolutely clear that these pills had no active ingredient and were made from inert substances, but we actually had 'placebo' printed on the bottle," says Kaptchuk. "We told the patients that they didn't have to even believe in the placebo effect. Just take the pills."

For a three-week period, the patients were monitored. By the end of the trial, nearly twice as many patients treated with the placebo reported adequate symptom relief as compared to the control group (59 percent vs. 35 percent). Also, on other outcome measures, patients taking the placebo doubled their rates of improvement to a degree roughly equivalent to the effects of the most powerful IBS medications.

"I didn't think it would work," says senior author Anthony Lembo, HMS associate professor of medicine at BIDMC and an expert on IBS. "I felt awkward asking patients to literally take a placebo. But to my surprise, it seemed to work for many of them."

The authors caution that this study is small and limited in scope and simply opens the door to the notion that placebos are effective even for the fully informed patient—a hypothesis that will need to be confirmed in larger trials.

"Nevertheless," says Kaptchuk, "these findings suggest that rather than mere positive thinking, there may be significant benefit to the very performance of medical ritual. I'm excited about studying this further. Placebo may work even if patients knows it is a placebo."

*This study was funded by the National Center for Complementary and Alternative Medicine and Osher Research Center, Harvard Medical School.*

**Citation:** *PLoS ONE*, December 22, 2010, online publication "**Placebos without deception: A randomized controlled trial in irritable bowel syndrome**"

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[http://www.eurekalert.org/pub\\_releases/2010-12/gumc-aas121710.php](http://www.eurekalert.org/pub_releases/2010-12/gumc-aas121710.php)

### **Arsenic agent shuts down 2 hard-to-treat cancers in animal experiments**

**The drug is already FDA-approved for one kind of cancer. Researchers say immediate clinical applications to treat other cancers is possible**

Washington, DC – Researchers at the Georgetown Lombardi Comprehensive Cancer Center, a part of Georgetown University Medical Center, have found that an arsenic-based agent already FDA-approved for a type of leukemia may be helpful in another hard-to-treat cancer, Ewing's Sarcoma (ES).

The research, based on animal studies, also suggests the drug might be beneficial in treating medulloblastoma, a highly malignant pediatric brain cancer.

In the December 22 issue of the *Journal of Clinical Investigation*, the investigators describe how years of research has uncovered a common pathway in these tumors, known as hedgehog/GLI1. They further detail how they used an existing drug, arsenic trioxide (Trisenox®), to shut down that pathway in mice models of ES and medulloblastoma.

This pathway is also common in other cancers, such as colon, pancreatic, and basal cell skin cancer, among others, says the study's lead investigator, associate professor Aykut Üren, M.D., of Georgetown Lombardi.

"The significance of our finding is that this FDA approved agent can be tested immediately in other cancer types. It is a perfect translational research project," he says. "This laboratory research has immediate clinical implications."

Üren adds that researchers are moving quickly to find an effective inhibitor of the hedgehog/GLI1 pathway because it is so powerful in cancer development. Hedgehog controls cell division in embryonic development, but when it is turned on, and out of control in adult cells, cancer results. Because of that, there are a number of clinical trials underway testing new compounds that inhibit this pathway at the surface membrane of cancer cells, he says.

The compound they tested, however, inhibits the pathway in the nucleus, so it may be effective in cancers that have pathway activation downstream of the membrane molecules, Üren says. "Many of the current clinical trials involve agents that act at the membrane. Ewing sarcoma and colon cancer will not benefit from that approach. Furthermore, medulloblastoma patients treated with hedgehog inhibitors are developing resistance at the membrane level. Therefore, clinical trials can evaluate alternative therapies for patients whose treatment fails with current hedgehog inhibitors," he says.

Arsenic trioxide has been approved for use of acute promyelocytic leukemia (APL) as a second-line therapy for patients who do not respond to standard therapy.

Arsenic trioxide is generated from processing arsenic compounds, and while a high level of arsenic is known to be carcinogenic, low doses can be therapeutic in selected patients, Üren says. In fact, he says starting in the 17th century, arsenic was the primary therapy for treating leukemia, specifically chronic myelogenous leukemia



(CML). He also cites a Dutch population study that concluded low levels of arsenic concentrations in drinking water not only didn't increase cancer incidence in people who drank it, but resulted in a decrease in nonmelanoma skin cancers.

"Like any chemotherapy, high doses of arsenic can be toxic, while lower doses can treat cancer," he says.

In 2009, Üren and his research team, which includes first author Elspeth Beauchamp, Ph.D., showed that the hedgehog/GLI1 pathway is activated in ES. They are now the first to inhibit this pathway by arsenic trioxide in ES, and among the first to show its activity in medulloblastoma.

*The study was funded by the National Institutes of Health, the Children's Cancer Foundation of Baltimore, and Accelerate Brain Cancer Cure. The authors report having no personal financial interests related to the study.*

[http://www.eurekalert.org/pub\\_releases/2010-12/ip-rtl122210.php](http://www.eurekalert.org/pub_releases/2010-12/ip-rtl122210.php)

### **Record time limit**

#### ***When will runners and swimmers reach their physical limit***

Running and swimming records are broken again and again at almost every international athletics event. But, can human performance continue to improve indefinitely? Will runners continue to accelerate off the starting blocks and reach the finish line in faster and faster times? Will swimmers always be able to dive into the record books with a quicker kick?

Writing in the International Journal of Applied Management Science, researchers from South Korea have analyzed data from sports events over the last one hundred years and have calculated that we could reach the upper limits on elite human performance within a decade.

Yu Sang Chang and Seung Jin Baek of the KDI School of Public Policy and Management in Seoul used non-linear regression models to accurately extrapolate the data from 61 running and swimming events. They have found the "time to limit" to be somewhere between 7.5 and 10.5 years. So, we may still see records being broken at the 2012 Olympics in London and perhaps at Rio 2016, but after that...who knows? The researchers believe their discovery of a "time to limit" has a number of policy implications for the local and national sport associations as well as for the international rule-setting federations.

Of course, US swimmer, Michael Phelps famously proclaimed that, "You can't put a limit on anything. The more you dream, the farther you get." Phelps has set around 40 world records. Sprinter Usain Bolt of Jamaica, similarly shaves split seconds from his 100-metre time almost every time he runs. Countless researchers have previously suggested that humans have a performance limit, Bolt's 9.58 second 100m shattered the previous theoretical running speed limit of 9.60s suggested 40 years ago.

"The limit of speed in sport events has been a popular topic for the public because watching athletes setting new records to win is exciting and stimulating for many sport fans," Chang and Baek suggest. "In addition, setting new world records may even be inspiring to the public because the process of improving and winning the competition reminds them of what they can accomplish in their own life."

Other researchers have criticized the use of linear regression to extrapolate to a limit. However, the present work uses the officially recognized world records on 61 sporting events during the period from 1900 to 2009. (29 running and 32 swimming events all at the Olympic level. "Therefore, this study may be the most comprehensive study undertaken so far," the researchers say. Their statistical analysis suggests that improvements in running and swimming are slowing down and will eventually reach a maximum in the time period they suggest. However, their analysis does not take into account changes in the rules, measurements, and environmental conditions. If the governing federations move the starting blocks as it were, Phelps' prediction that there are no limits may come true and athletes will continue to make a splash in the record books indefinitely.

*"Limit to improvement in running and swimming" Int. J. Applied Management Science, 2011, 3, 97-120*

<http://news.discovery.com/earth/cold-winter-snow-weather-global-warming-101222.html>

### **Cold Winters Driven By Global Warming**

#### ***Melting Arctic ice is to blame for the change in weather patterns, scientists say.***

Counterintuitive but true, say scientists: a string of freezing European winters scattered over the last decade has been driven in large part by global warming. The culprit, according to a new study, is the Arctic's receding surface ice, which at current rates of decline could disappear entirely during summer months by century's end.

The mechanism uncovered triples the chances that future winters in Europe and north Asia will be similarly inclement, the study reports.

Bitingly cold weather wreaked havoc across Europe in the winter months of 2005-2006, dumping snow in southern Spain and plunging eastern Europe and Russia into an unusually -- and deadly -- deep freeze.

Another sustained cold streak in 2009-2010, gave Britain its coldest winter in 14 years, and wreaked transportation havoc across the continent. This year seems poised to deliver a repeat performance.

At first glance, this flurry of frostiness would seem to be at odds with standard climate change scenarios in which Earth's temperature steadily rises, possibly by as much as five or six degrees Celsius (9.0 to 10.8 degrees Fahrenheit) by 2100. Climate skeptics who question the gravity of global warming or that humans are to blame point to the deep chills as confirmation of their doubts. Such assertions, counter scientists, mistakenly conflate the long-term patterns of climate with the short-term vagaries of weather, and ignore regional variation in climate change impacts.

New research, however, goes further, showing that global warming has actually contributed to Europe's winter blues. Rising temperatures in the Arctic -- increasing at two to three times the global average -- have peeled back the region's floating ice cover by 20 percent over the last three decades.

This has allowed more of the sun's radiative force to be absorbed by dark-blue sea rather than bounced back into space by reflective ice and snow, accelerating the warming process.

More critically for weather patterns, it has also created a massive source of heat during the winter months.

"Say the ocean is at zero degrees Celsius (32 degrees Fahrenheit)," said Stefan Rahmstorf, a climate scientist at the Potsdam Institute for Climate Impact Research in Germany. "That is a lot warmer than the overlying air in the polar area in winter, so you get a major heat flow heating up the atmosphere from below which you don't have when it is covered by ice. That's a massive change," he told AFP in an interview.

The result, according to a modeling study published earlier this month in the *Journal of Geophysical Research*, is a strong high-pressure system over the newly exposed sea which brings cold polar air, swirling counter-clockwise, into Europe. "Recent severe winters like last year's or the one of 2005-2006 do not conflict with the global warming picture, but rather supplement it," explained Vladimir Petoukhov, lead author of the study and a physicist at the Potsdam Institute.

"These anomalies could triple the probability of cold winter extremes in Europe and north Asia," he said.

The researchers created a computer model simulating the impact on weather patterns of a gradual reduction of winter ice cover in the Barents-Kara Sea, north of Scandinavia.

Other possible explanations for uncommonly cold winters -- reduced sun activity or changes in the Gulf Stream -- "tend to exaggerate their effect," Petoukhov said. He also points out that during the freezing 2005-2006 winter, when temperatures averaged 10 degrees Celsius below normal in Siberia, there were no unusual variations in the north Atlantic oscillation, another putative cause.

Colder European winters do not indicate a slowing of global warming trends, only an uneven distribution, researchers say. "As I look out my window I see about 30 centimeters of snow and the thermostat reads -14.0 degrees Celsius," said Rahmstorf, speaking by phone from Potsdam.

"At the same time, in Greenland we have above zero temperatures -- in December."

<http://news.nationalgeographic.com/news/2010/12/101221-solar-power-hornet-science-animals/>

### **Solar-Powered Hornet Found; Turns Light Into Electricity**

***In an animal kingdom first, insect's "skin" pigments convert sunlight into energy.***

**Matt Kaplan for National Geographic News**

The oriental hornet has built-in "solar cells" that generate electricity from sunlight—a first in the animal kingdom, according to a new study. Scientists already knew that the hornet species, for unknown reasons, produced electricity inside its exoskeleton, according to study leader Marian Plotkin of Tel-Aviv University. Plotkin's late mentor Jacob Ishay made the discovery after observing that the insect is active when the sun is most intense—unusual for hornets.

Plotkin and colleagues recently went a step further by examining the structure of the hornet's exoskeleton to find out how the electricity is produced. Their research revealed that pigments in the hornet's yellow tissues trap light, while its brown tissues generate electricity. Exactly how the hornets use this electricity is still not entirely understood, Plotkin noted. "When I was running my experiment, people told me it was never going to work," she said. "I'm so happy at the results."



***The oriental hornet's colors contain power-producing pigments (file picture). Photograph by Blickwinkel, Alamy***

While solar cells using human-made substances are usually 10 to 11 percent efficient at generating electricity, the hornet's cells are only 0.335 percent efficient. For instance, the hornet still gets the vast majority of its energy from food. But that's hardly the point, Plotkin said. "We've seen solar harvesting in plants and bacteria, but never before in animals."

#### **Hornet Pigment a Solar Power Source**

The team found that many of the hornet's brown tissues contain melanin, the pigment that protects human skin cells by absorbing damaging ultraviolet light and transforming it into heat. A structural analysis of the

brown tissues also uncovered grooves that capture light by channeling rays into the tissues and breaking them apart into smaller rays. The brown tissues "are a lot like a light trap—only one percent of the light that strikes is reflected away," said Plotkin, whose study appeared in the December issue of the journal *Naturwissenschaften*.

The hornet's yellow tissues contained the obscure pigment xanthopterin, which gives butterfly wings and mammal urine their color. ([\*Read about a urine battery that turns pee into power.\*](#))

When the team isolated xanthopterin in a liquid solution, and then placed the solution inside a solid solar cell electrode, a type of conductor. When the scientists shed light on the electrode, the pigment in the solution generated electricity.

### **"Fabulous" Hornet Study Needs Comparison**

Entomologist Chris Lyal at London's Natural History Museum called the study a "fabulous investigation."

"I'd love to see a comparison with the [exoskeleton] structure of other hornets that do not appear to be gathering energy from the sun. In theory, other hornets should have exoskeleton layers that look very different," said Lyal, who was not involved in the study. It's also possible other insects have similar electricity-generating abilities, Lyal added. "For instance, I remember coming across the Apollo butterfly in the Pyrenees, which basks in the sun before flying—presumably absorbing solar radiation," he said.

"I wonder how different the hornet tissues actually are from those of that butterfly."

<http://www.nature.com/news/2010/101221/full/4681011a.html>

### **Love thy lab neighbour**

#### ***Getting closer to your collaborators boosts a paper's citations.***

**Richard Van Noorden**

Anyone who has worked in a laboratory probably feels that having key members of the group placed closer together makes for a better research project. A study linking the proximity of investigators and the impact of their research now backs up that hunch.

Isaac Kohane, co-director of the Harvard Medical School Center for Biomedical Informatics in Boston, Massachusetts, decided to put intuition to the test in 2005 after a debate with Harvard's dean of administration, Richard Mills, over the layout of the centre. "I felt this viscerally, but there was no hard evidence," says Kohane. He enlisted more than a dozen undergraduates to identify 35,000 articles published between 1999 and 2003 in biomedical sciences, each with at least one Harvard author.

It took the team two years to pinpoint where individual Harvard investigators were working — right down to the level of individual offices and laboratories.

The results, published in PLoS ONE last week (K. Lee et al. PLoS ONE 5, e14279; 2010), show that the shorter the geographical distance between first and last authors on a paper, the more highly cited were their research papers. First authors often bear the brunt of the work, whereas last authors tend to take the lead organizational role — and both are key players in the research project. The distance trend was not found for middle authors, who could be far removed from other collaborators without any clear effect on research impact.

Kohane and his colleagues also looked at individual buildings on the four campuses across which Harvard life-science research happens to be spread.

They found that the more that researchers within a building tended to collaborate with one another rather than with people elsewhere, the more highly cited the publications that came from that building (see picture). The team does acknowledge an alternative explanation for the data: that scientists might choose to keep potentially high-impact breakthroughs within their own laboratory, or within a close circle of researchers.

This seems to be the first empirical study of the connection between proximity and impact, says Anthony van Raan, an expert in using citation analyses to study scientific productivity and impact at Leiden University, the Netherlands. Most studies of the relationship between spatial separation and scientific impact have been done on a national and international scale, for which it has been demonstrated many times that international collaborations produce more highly cited science than local collaborations — probably a consequence of the size and scope of such efforts.

Kohane speculates that international collaborations might become even more successful if the first and last authors worked very close together, something that has not yet been tested. He certainly practises what he preaches: he and first author Kyungjoon (Joon) Lee, who coordinated the undergraduates' fact-finding, now work on the same floor. "When the study started we were on different floors," says Kohane, "and Joon told me that I became a lot more helpful when I moved to his floor."

## GP report flu cases have doubled in one week

By Helen Briggs Health reporter, BBC News

### Officials are urging patients in high-risk groups to get immunised

The biggest increase is in school age children, data from GP surgeries shows.

Several flu strains are known to be circulating widely, including H1N1 "swine flu" and influenza B.

Experts are urging those in high-risk groups, particularly pregnant women, to get vaccinated. The vaccine protects against both seasonal flu and swine flu.

The figures come from [The Royal College of GPs](#), which tracks cases of flu-like illnesses at about 70 surgeries in England and Wales.

Cases have risen to 87.1 per 100,000 people, from 32.8 in the previous week. This falls far short of the number of people catching flu at the height of last summer's swine flu outbreak. But it is higher than seasonal flu outbreaks of the past few years.

"There's a fair bit of flu around but we're not overwhelmed by it," Dr Maureen Baker, Health Protection Lead at the Royal College of GPs, told the BBC.

Rates of flu are highest in children aged between 5 and 14, followed by children under four, then those aged between 15 and 44.

Professor Hugh Pennington, an expert in viruses, said it is very worrying that many people at risk of flu are not being vaccinated.

Cases have also increased in adults aged between 45 and 64, says the weekly bulletin from the Royal College of GPs. The Central region (including Wales) has the most cases, followed closely by the South, with fewer cases in the North. It is not clear how many of these patients have H1N1 flu, influenza B and other strains.

### Hospital cases

On Tuesday, it was revealed there had been a rise in the numbers of people admitted to intensive care with flu.

Government figures show that 302 beds are now occupied by flu patients.

Professor Peter Openshaw of the National Heart & Lung Institute, Imperial College London, said there was no evidence the virus had changed. "From around the country, reports from frontline staff are showing unprecedented levels of hospitalisation with severe flu in high-risk adults. "All the evidence we have so far is that the virus has not changed. "It is affecting the same type of person as last year and still behaves like swine flu rather than normal seasonal flu (which mostly affects the over 65s)."

A Department of Health spokesperson said the figures were "in keeping with what we would expect during a winter flu season". "But everyone can do their bit to help keep well - simple measures like washing your hand help stop flu spreading.

"The Chief Medical Officer has issued clear advice to get the seasonal flu jab If you are in a vulnerable group, particularly pregnant women and people with underlying health condition, as well as those aged 65 and over."

The latest information on the number of deaths from seasonal flu and swine flu will be released by the Health Protection Agency on Thursday.

Updated figures on levels of seasonal flu circulating in Scotland are also due to be released that day.

<http://www.scientificamerican.com/article.cfm?id=disaster-doctors-may-be-using->

## Disaster Doctors May Be Using the Wrong Drugs

### Study of Haiti earthquake victims shows most wounds infected with Gram-negative, not Gram-positive, bacteria.

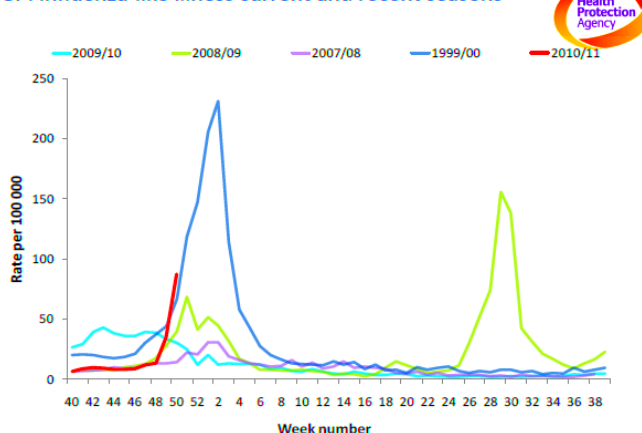
By Daniel Cressey

Guidelines for medical teams responding to catastrophes such as the Haiti earthquake may be causing doctors to miss a crucial set of deadly bacteria.

According to an Israeli Defense Forces (IDF) rapid-response team, a large proportion of the wounds treated at their field hospital in Haiti were infected with Gram-negative pathogens. These bacteria are largely ignored in current recommendations on drug treatment for disaster victims.

Staining with the dye crystal violet is widely used to differentiate bacteria into two types -- Gram-positive and Gram-negative -- in a procedure developed in the nineteenth century by Hans Christian Gram. Crucially, drugs that are effective against one type of bacteria may not work against the other.

RCGP: Influenza-like illness current and recent seasons



Guidelines from the World Health Organization (WHO) and from the US Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, recommend treating injured patients with antimicrobials that target Gram-positive bacteria, as these strains are the most common cause of wound infections. But what is the case in hospitals in the West doesn't necessarily hold for the extreme conditions following a disaster.

"Skin and soft-tissue injuries are usually associated with Gram-positive pathogens and thus the previous guidelines seemed reasonable," says Ian Miskin, a doctor with the Clalit Health Services organization based in Jerusalem, and who was part of the rapid-response team. "However, after lying in the rubble for hours to days after an earthquake it appears that the pathogens causing wound infections were Gram-negative -- possibly due to wound contamination with fecal material."

In the immediate aftermath of the earthquake that devastated Haiti in January, the IDF set up a 72-bed mobile hospital. Over ten days the hospital admitted 737 victims of the disaster.

Miskin's team set up an on-site microbiology laboratory which analysed cultures taken from patients with infected wounds. They found that 77% of 46 wounds analysed contained multiple types of microbe, with 89% showing Gram-negative pathogens.

These Gram-negative bacteria were also mostly resistant to antimicrobials recommended by the CDC and WHO disaster-response guidelines, the researchers note in a letter in this week's *New England Journal of Medicine*.

Miskin, lead author of the letter, adds, "If teams responding to future earthquakes do not equip themselves with appropriate antibiotics they may be unable to treat the wound infections resulting from the earthquake damage."

He stresses the vital importance of on-site microbiology, which allows doctors to tailor their treatments to the local pathogens found in victims.

### **Recommended responses**

Previous studies have indicated that Gram-negative bacteria are present in wounds in most disaster victims. However, these studies focused on referral hospitals and patients who had already received antibiotic treatment. So it was always possible that the bacteria were present as a result of hospital contamination or of the initial antibiotic treatment wiping out the Gram-positive bacteria.

Andrew Lee, a doctor and researcher in disaster response and international health at the University of Sheffield, told *Nature* that Miskin's report is "a timely piece and of considerable implications for current medical practice in disaster settings".

However, he warns that, although microbiological tests carried out in the field are hugely valuable, they are logistically very difficult. An alternative solution is that doctors could treat first with a short course of penicillins, which are effective against Gram-positive infections, then follow up with drugs that target Gram-negative bacteria if the initial treatment is ineffective.

Richard Murphy, a medical advisor to Médecins Sans Frontières (MSF), says that his organization did stress the importance of Gram-negative infections in its guidance to Haiti responders, but says that there needs to be a wider appreciation of the problem. "In soft tissue and bone infections in warm countries we've known for some time that Gram-negative organisms can be as important or more important than Gram-positive infections."

The WHO was unable to comment before this article was published. The CDC said that it does not comment on non-CDC authored articles.

[http://www.eurekalert.org/pub\\_releases/2010-12/dci-gai122010.php](http://www.eurekalert.org/pub_releases/2010-12/dci-gai122010.php)

### **Gene alteration in mice mimics heart-building effect of exercise Suggests potential strategy for repairing injured hearts**

BOSTON--By tweaking a single gene, scientists have mimicked in sedentary mice the heart-strengthening effects of two weeks of endurance training, according to a report from Dana-Farber Cancer Institute and Beth Israel Deaconess Medical Center (BIDMC). The genetic manipulation spurred the animals' heart muscle cells -- called cardiomyocytes -- to proliferate and grow larger by an amount comparable to normal mice that swam for up to three hours a day, the authors write in the journal *Cell*. This specific gene manipulation can't be done in humans, they say, but the findings may suggest a future strategy for repairing injured hearts through muscle regeneration.

"If we learned to manipulate this pathway with specific exercise regimens or with drugs, we might be able to achieve some of the benefits produced by exercise-related heart enlargement," said Bruce Spiegelman, PhD, of Dana-Farber, the study's co-senior author with Anthony Rosenzweig, MD, of BIDMC. Pontus Bostrom, PhD, MD, a postdoctoral fellow at Dana-Farber, is the first author.

The investigators found that the mildly enlarged hearts of the genetically altered mice proved to be surprisingly resistant to a model of cardiac stress that mimics valvular heart disease or the effects of high blood pressure. Someday this observation might lead to therapeutic measures to treat or prevent heart failure, Spiegelman said.

Only recently have scientists discovered that adult cardiomyocytes retain the potential to begin dividing and spawning new muscle cells. In their new publication, the authors describe for the first time a genetic trigger that responds to physical exercise and turns on a molecular pathway that jump-starts cardiomyocyte growth.

"It's well documented that exercise has beneficial effects on metabolism and skeletal muscle, but we hypothesized that it might also have more direct beneficial effects in the heart itself that could be exploited to protect against heart failure," noted Rosenzweig, a cardiologist at BIDMC.

While most previous studies have investigated diseased hearts, these investigators focused their studies on the changes that occur in hearts after endurance exercise. Heart muscle enlargement, or hypertrophy, in response to exercise is popularly known as "athlete's heart" in humans. This process of benign heart muscle growth, the scientists found, involves a distinctly different series of molecular events from those causing pathological hypertrophy -- the enlarged and damaged heart seen in patients suffering from factors like high blood pressure.

While the molecular networks involved in pathological hypertrophy have been studied extensively, there's been little research on the pathways leading to benign heart enlargement, despite the fact that "exercise protects the heart at so many levels," said Bostrom. "We decided to try and find a gene that could be driving some of the important changes we see in exercise."

First, they had adult mice swim daily for increasing amounts of time, and after 14 days found that their hearts were mildly enlarged as a result. Other mice with restricted blood flow in their aorta also showed enlargement, but of the type associated with heart disease. The researchers then screened both sets of animals against a collection of all known transcription factors -- proteins that turn gene activity up or down -- and compared their expression in the two types of heart enlargement.

The key differences turned out to be in a pair of transcription factors acting in concert. One, C/EPB-beta, had reduced activity in the exercised mice while the other, CITED4, was more active.

So, could turning down C/EPB-beta in normal mice cause their hearts to grow as if they had been working out -- even though they did no extra exercise? The answer was yes: Genetic manipulation to reduce C/EPB-beta expression raised the activity of CITED4, and in those mice, cardiomyocytes began dividing and growing in size until their heart muscles resembled those of the endurance swimmers. The mice also had markedly improved maximal exercise capacity even without exercise training.

Importantly, lowering C/EPB-beta expression also protected mice from developing heart failure as a result of restricted aortic blood flow. It is likely that the more-robust cardiomyocytes played an important role in the resistance to heart failure, said the investigators, but they couldn't rule out that other actions of reduced C/EPB-beta and increased CITED4 also contributed.

The authors concluded that developing greater insight into the pathways affecting C/EPB-beta protein expression, or drugs that suppress C/EPB-beta expression in the heart, could be of significant clinical value. "By understanding the pathways that benefit the heart with exercise, we may be able to exploit those for patients who aren't able to exercise," said Rosenzweig. "If there were a way to modulate the same pathway in a beneficial way, it would open up new avenues for treatment."

*Other authors are from Dana-Farber, BIDMC, and Brigham and Women's Hospital.*

*Support for the research was provided in part by the Leducq Foundation Network of Research Excellence and the National Institutes of Health.*

<http://www.bbc.co.uk/news/science-environment-12008573>

### **Biochar: Running the numbers**

**Richard Black By Richard Black Environment correspondent, BBC News**

***In search of a "magic bullet" for climate change that will simultaneously help with the growing problem of feeding the world, gurus from James Lovelock downwards have praised the potential of biochar.***

"I said in my recent book that perhaps the only tool we had to bring carbon dioxide back to pre-industrial levels was to let the biosphere pump it from the air for us," the originator of the Gaia concept told The Guardian newspaper last year. "We don't need plantations or crops planted for biochar, what we need is a charcoal maker on every farm so the farmer can turn his waste into carbon."

But will farmers want to? Will it be worth their while?

Dr Lovelock would presumably be encouraged by developments at Stonelaws Farm in Scotland, whose owner Colin Hunter is taking a close look at the potential and pitfalls of biochar, in conjunction with researchers from the UK Biochar Research Centre at nearby Edinburgh University.

The project is helping to answer some of the big outstanding questions: for how long does biochar lock carbon into the soil, how much benefit does it produce for crops, how does it stack up against other uses for waste, and how can it be tailored to produce maximum benefits?

And those answers in turn could help determine whether biochar does turn into a worldwide phenomenon, or whether it eventually finds its way into the bin marked "Good Idea - But..."

### **Winning ways**

At first sight, the case for biochar seems unanswerable; a win-win-win-win-win situation.

Charcoal making Modern biochar production is a more efficient variant of tradition charcoal making

Plant waste is heated to temperatures of several hundred Celsius in a pyroliser, a vessel from which oxygen is excluded; so it does not burn. Instead, gases and liquids are driven off, which can potentially be used as fuel or agricultural treatments. The remainder turns into a dry, carbon-rich solid similar to charcoal.

Scattered on fields, biochar helps raise crop yields; and the carbon it contains is locked away for thousands of years. As that carbon had been absorbed from the atmosphere as the plants grew, what we have is a net removal of carbon from the atmosphere and storage in soil. So we have improved crop yields, carbon storage, virtually free fuel, waste disposal and potentially extra earnings for the farmer as well; what is not to like?

Academic backing emerged a few months ago with the publication of a study showing that biochar could absorb 12% of humanity's greenhouse gas emissions - not a complete bullet, perhaps, but certainly a valuable weapon for the anti-climate change armoury.

On the other hand, bad experiences from the "race to biofuels" and the UN's Clean Development Mechanism (CDM) mean there are concerns that biochar could be practised, or rewarded, inappropriately, with "perverse incentives" emerging that could reward logging for biochar or the indiscriminate spreading of char on crops that would not benefit. Hence the need for more research.

The technique is being adopted on a small scale in many countries, but many of the basic questions remain unresolved - hence the importance of the Stonelaws Farm site.

"I was brought up on a farm and we had an 'ash field' where we used to take ash from houses in the village and put it on the field," Mr Hunter recalls. "That was a much more fertile part of the field than the rest, and there was some charcoal in the ash and obviously it was having an effect. So I wanted to see if that could be replicated." Hence his enthusiasm for hosting the biochar project, run by Jason Cook.

### **Machine head**

The char is made in what looks at first sight like a boiler - a machine about as tall as a person, adorned with pipes, a bucket hanging from one of them. It is a pyroliser - Indian-made - a fairly low-tech item designed for practical use rather than fancy laboratory experimentation.

Jason shows me the raw material - fragments of Scots pine or willow - and the blackened, dry residue it turns into during its voyage through the pyroliser. Then he dumps a sackful of wood into it, locks down the lid to keep the air out, and fires the beast up. For the next 20 minutes or so we see the temperature rise to several hundred Celsius - he has taken it as far as 650C.

Gradually, puffs of something appear from the pipe. Not smoke, because the wood is not burning - rather, the first of the gases that are being driven off, mostly water vapour with a cargo of brown stuff. Meanwhile, the first liquid emerges from the condenser pipe - a pungent, oily brew that can be used as a herbicide.

Jason then holds a match to the gas pipe and it struggles into a flame, becoming more stable as the proportion of methane and hydrogen rises with the temperature. "The next stage is to collect the gas and get it analysed back in the lab, and get the calorific value," Jason explains. "We want to see if there's an optimal temperature where we're getting the most valuable flammable gas coming off."

Colin Hunter spends about £20,000 per year on gas that is burned to dry grain - and one of the benefits of pyrolysis could be to produce enough gas that he can keep this money in his pocket.

### **On fertile ground**

The solid left at the end of the pyrolysis process is spread on fields to see whether biochar does boost crop yields as claimed. "I'm harvesting with a combine harvester that combines GPS tracking with very accurate yield measurement, so we can get a very good view on this," Jason relates. "Last year we spread 10 tonnes per hectare on spring barley, and got a statistically significant yield increase of 7%."

More recent results indicate that higher yield increases are possible, but also that there is a threshold; spread too much, and the yield goes down again.

What complicates the analyses of these effects is that it is not entirely clear what biochar does in the soil.

"It's largely carbon and very porous, so maybe it's creating a home for microbial communities," Jason says.

"It may also aerate the soil and assist with water-logging.

"The carbon has got a nutrient value itself, and it's been shown to stop some other nutrients like nitrates leaching away, which suggests using it is going to allow you to reduce the amount of fertiliser you need."

## Bespoke biochar

The labs at Edinburgh University hold a cache of samples that may, in time, show how to make biochar for maximum impact: how hot to run the pyroliser, how long to leave the wood inside, and what sort of soils and crops will benefit the most. "The higher the temperature, the more of the volatile liquids and gases you drive off, so the lower yield of char you get," explains researcher Pete Brownsort.

"But it may be more stable char - or it might not be - that's a big question at this time.

Pyroliser The pyroliser produces flammable liquid and gas, which could be used as fuels on the farm

"At this centre we have the concept of 'bespoke biochar', which is an idea of producing the char that's going to have the exact properties you'll need in the field where you're going to use it."

According to this vision - developed by Edinburgh soil scientist Saran Sohi - you could give farmers a recipe book allowing them to make precisely what char they need, bearing in mind that they may be looking for a balance of yield increases from the char and fuel from the gas and liquid. Potentially this could also allow authorities to reward farmers for capturing and storing carbon - and to know how much they should pay the farmers.

In the case of Stonelaws Farm, the economics are as yet unclear, according to Colin Hunter - and complicated by the fact that farm waste going into the pyroliser could instead be burned, producing a greater dividend in heat and potentially in electricity generation too.

"You'd have to be seeing fairly dramatic increases in crop yields, otherwise you'd say 'well we'll just chop up the straw and put it back on the fields instead of bringing it in, heating it and taking it back out again'," he says.

"The other aspect to this though is carbon credits. "If we could earn carbon credits for this, it would transform the viability; and if we generate electricity, do we qualify for the feed-in tariff?"

Research at Edinburgh and elsewhere has shown that the carbon economics of biochar can stack up rather well.

In contrast to burning, about half of the carbon in the waste is captured and stored; meanwhile, the liquids and gases yield easily enough energy to power the pyroliser, with some left over for other uses around the farm.

But you sense biochar will take off only if and when farmers believe they have something to gain from it economically as well; and on a global scale, that case remains complex and unproven.

You can find out more about the potential of biochar and other technological "climate fixes" in [this week's edition of One Planet](#) on the BBC World Service.

<http://www.newscientist.com/article/dn19902-did-martian-methane-signal-come-from-earth.html>

### **Did 'Martian' methane signal come from Earth?**

**\* 11:46 23 December 2010 by Rachel Courtland**

***Claims that Mars's atmosphere contains methane, which have fuelled speculations that the planet hosts life, may be premature.***

A key piece of evidence for methane on Mars may actually be due to Earth-based methane, say researchers led by Kevin Zahnle of the NASA Ames Research Center in Moffett Field, California. "This is not a done deal," says Zahnle, despite a widespread perception that methane has been found on the Red Planet.

The clearest evidence for methane on Mars came in 2009 from a team led by Michael Mumma at NASA's Goddard Space Flight Center in Greenbelt, Maryland. They used ground-based telescopes to look at light emitted by Mars and attributed dips in the spectrum to martian methane absorbing those frequencies.

The readings, taken several years apart, suggested that methane's lifetime in the Martian atmosphere is unexpectedly – and inexplicably – short. While most researchers have assumed that this was due to an as-yet-unknown Martian process, Zahnle's team offers an alternative explanation: the dips in the spectrum are not due to alien methane.

### **Spectral dips**

Mumma's team focused on readings taken when Mars was either moving toward or away from Earth, when any dips in its light would be shifted to higher or lower frequencies and so could be separated from dips caused by methane in Earth's atmosphere. But Zahnle's team notes that the frequency of a spectral dip attributed to Martian methane could also be caused by earth-based methane containing carbon-13 instead of the more common carbon-12 isotope.

Mumma says he and his colleagues were careful in subtracting off these signals from Earth's atmosphere and are confident that they are measuring Martian methane.

Since the team detected hotspots of methane instead of a single methane signal spread across the planet, Mumma says, that also suggests the methane signal does not come from a haze of the gas hovering in Earth's atmosphere.



## Future tests

The team's first signals of methane came in 2003, and "we spent five years learning how to better interpret the results. My group does not publish until we're certain we've exhausted all other possible explanations," Mumma says. "That being said, there can always be some hidden assumption or hidden error that one does not anticipate or notice, so for that reason alone we welcome the attention."

Clearer answers to the methane question may be on the way soon, with the launch of NASA's Mars Science Laboratory (MSL) rover in 2011 and a joint NASA-ESA orbiter called the Trace Gas Orbiter scheduled for launch in 2016.

In June, Mumma and colleagues also finished a 10-month-long campaign to hunt for Martian methane using three large telescopes in Chile and Hawaii. They hope to have new methane results in a few months to help NASA whittle down a set of four potential landing sites for MSL. The rover is set to launch in November 2011.

*Journal reference: Icarus, DOI: 10.1016/j.icarus.2010.11.027*

<http://www.physorg.com/news/2010-12-ingestion-starch-malaria-vaccine-strategy.html>

### **Could the ingestion of 'modified' starch be a new malaria vaccine strategy?**

***There is no efficient vaccine against malaria, although nasal and oral vaccination seems to be the most promising and suitable solution in countries where the parasite Plasmodium, which causes the disease, is rife. Researchers from two laboratories in northern France have successfully vaccinated and protected mice by feeding them starch derived from green algae and genetically modified to carry vaccine proteins.***

These encouraging results, which make it possible to envisage a simple and safe vaccination for children in countries at risk, are available online, on the scientific journal PloS One's website.

According to the WHO, malaria affects approximately 300 to 500 million people worldwide and kills one million each year, mostly young children. Insecticide-resistant mosquitoes carrying the disease and multi-drug resistant parasites are on the increase. In this context, the development of a vaccine that alleviates symptoms and reduces mortality would be a valuable new tool in the fight against malaria.

Researchers aim to test the efficacy of vaccine candidates among proteins that allow the parasite to penetrate host cells and infect them, in order to devise the best strategy for vaccine delivery.

Researchers from the Centre d'Infection et d'Immunité de Lille and the Unité de Glycobiologie Structurale et Fonctionnelle have developed a new vaccine strategy based on the ingestion of genetically modified starch. They used antigens that have shown their efficacy in "conventional" vaccinations as vaccine candidates. They fused these antigens to an enzyme (GBSS) in a starch granule from the green algae, *Chlamydomonas reinhardtii*.

This enzyme has the particularity of functioning inside the starch granule and of being protected, along with the antigens grafted to it, against degradation by other enzymes. In this way, the researchers were able to produce several murine and human antigens of *Plasmodium* within starch grains. These grains were then ingested by mice inoculated with the parasite.

The researchers demonstrated that the mice were vaccinated by the starch grains, which significantly protected them against infection.

Starch is the insoluble and semi-crystalline polysaccharide that is the most commonly found in photosynthetic organisms. A starch grain can easily be produced from a plant extract and purified, in large quantities. It has a very stable structure and can be stored for months with no particular precaution, even if it undergoes temperature variations. It is easily assimilated through digestion and has a major ecological and financial interest, with very low production costs.

The starch of edible plants could be transformed in the same way as that of the algae *Chlamydomonas reinhardtii*. Researchers are thus looking at the possibility of using starch from multi-cellular algae used in Africa as a food supplement, but also from maize and potatoes.

Administered to children under 3 years of age, who are at high-risk of malaria-related mortality, such plants could be both a food source and a vaccine. This strategy would allow simple vaccination, avoid storage problems and syringes, and thus eliminate potential HIV contamination.

The vaccine strategy based on the ingestion of genetically modified starch is protected by a patent.

The researchers now plan to test the efficacy of various *Plasmodium* antigens and determine whether such strategy can be applied to humans by verifying it has no side effects.

*More information: PloS One, 15 December 2010: [http://www.plosone ... pone.0015424](http://www.plosone...pone.0015424) . Provided by CNRS*

## New solar fuel machine 'mimics plant life'

By Neil Bowdler Science reporter, BBC News

**A prototype solar device has been unveiled which mimics plant life, turning the Sun's energy into fuel.**

The machine uses the Sun's rays and a metal oxide called ceria to break down carbon dioxide or water into fuels which can be stored and transported. Conventional photovoltaic panels must use the electricity they generate in situ, and cannot deliver power at night. Details are published in the journal *Science*.

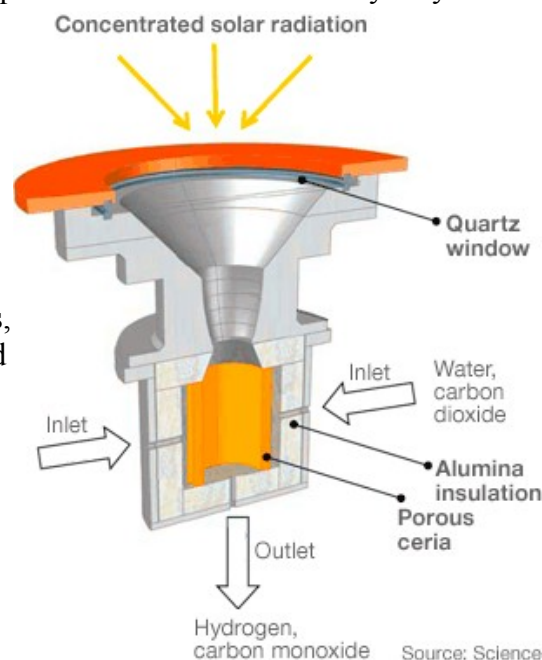
The prototype, which was devised by researchers in the US and Switzerland, uses a quartz window and cavity to concentrate sunlight into a cylinder lined with cerium oxide, also known as ceria.

Ceria has a natural propensity to exhale oxygen as it heats up and inhale it as it cools down.

If as in the prototype, carbon dioxide and/or water are pumped into the vessel, the ceria will rapidly strip the oxygen from them as it cools, creating hydrogen and/or carbon monoxide. Hydrogen produced could be used to fuel hydrogen fuel cells in cars, for example, while a combination of hydrogen and carbon monoxide can be used to create "syngas" for fuel.

It is this harnessing of ceria's properties in the solar reactor which represents the major breakthrough, say the inventors of the device. They also say the metal is readily available, being the most abundant of the "rare-earth" metals. Methane can be produced using the same machine, they say.

***In the prototype, sunlight heats a ceria cylinder which breaks down water or carbon dioxide***



### Refinements needed

The prototype is grossly inefficient, the fuel created harnessing only between 0.7% and 0.8% of the solar energy taken into the vessel. Most of the energy is lost through heat loss through the reactor's wall or through the re-radiation of sunlight back through the device's aperture. But the researchers are confident that efficiency rates of up to 19% can be achieved through better insulation and smaller apertures. Such efficiency rates, they say, could make for a viable commercial device.

"The chemistry of the material is really well suited to this process," says Professor Sossina Haile of the California Institute of Technology (Caltech). "This is the first demonstration of doing the full shebang, running it under (light) photons in a reactor."

She says the reactor could be used to create transportation fuels or be adopted in large-scale energy plants, where solar-sourced power could be available throughout the day and night.

However, she admits the fate of this and other devices in development is tied to whether states adopt a low-carbon policy. "It's very much tied to policy. If we had a carbon policy, something like this would move forward a lot more quickly," she told the BBC.

It has been suggested that the device mimics plants, which also use carbon dioxide, water and sunlight to create energy as part of the process of photosynthesis. But Professor Haile thinks the analogy is over-simplistic.

"Yes, the reactor takes in sunlight, we take in carbon dioxide and water and we produce a chemical compound, so in the most generic sense there are these similarities, but I think that's pretty much where the analogy ends."

Daniel Davies, chief technology officer at the British photovoltaic company Solar Century, said the research was "very exciting".

"I guess the question is where you locate it - would you put your solar collector on a roof or would it be better off as a big industrial concern in the Sahara and then shipping the liquid fuel?" he said.

Solar technology is moving forward apace but the overriding challenges remain ones of efficiency, economy and storage. New-generation "solar tower" plants have been built in Spain and the United States which use an array of mirrors to concentrate sunlight onto tower-mounted receivers which drive steam turbines.

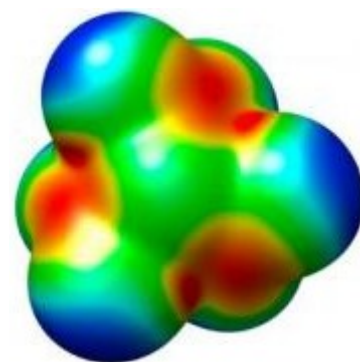
A new Spanish project will use molten salts to store heat from the Sun for up to 15 hours, so that the plant could potentially operate through the night.

## Discovery of new molecule can lead to more efficient rocket fuel

**Trinitramid – that's the name of the new molecule that may be a component in future rocket fuel. This fuel could be 20-30 percent more efficient in comparison with the best rocket fuels we have today. The discovery was made at the Royal Institute of Technology (KTH) in Sweden.**

"A rule of thumb is that for every ten-percent increase in efficiency for rocket fuel, the payload of the rocket can double. What's more, the molecule consists only of nitrogen and oxygen, which would make the rocket fuel environmentally friendly. This is more than can be said of today's solid rocket fuels, which entail the emission of the equivalent of 550 tons of concentrated hydrochloric acid for each launch of the space shuttle," says Tore Brinck, professor of physical chemistry at KTH.

Working with a research team at KTH, he discovered a new molecule in the nitrogen oxide group, which is not something that happens every day. It was while the scientists were studying the breakdown of another compound, using quantum chemistry computations, that they understood that the new molecule could be stable.



**Trinitramid -- that's the name of the new molecule that may be a component in future rocket fuel.** Credit: KTH, the Royal Institute of Technology Sweden

"As mentioned, what is specific to this molecule is that it contains only nitrogen and oxygen. Only eight such compounds were previously known, and most of them were discovered back in the 18th century. This is also clearly the largest of the nitrogen oxides. Its molecular formula is  $N(NO_2)_3$ , and the molecule is similar to a propeller in shape," says Tore Brinck.

The research team, consisting of Martin Rahm and Sergey Dvinshikh as well as Professor Istvan Furó, besides Tore Brinck, has now shown how the molecule can be produced and analyzed. The scientists have also managed to produce enough of the compound in a test tube for it to be detectable.

"It remains to be seen how stable the molecule is in a solid form," says Tore Brinck. It was during work to find an alternative to today's solid rocket fuel that the researchers found the new molecule. The findings are now being published in the respected journal *Angewandte Chemie International Edition*.

More information: <http://onlinelibrary.wiley.com/doi/abs/10.1002/anie.2010047> Provided by Swedish Research Council

<http://www.scientificamerican.com/blog/post.cfm?id=why-is-the-north-magnetic-pole-racing-toward-siberia-2010-12-24>

## Why is the north magnetic pole racing toward Siberia?

By John Matson | Dec 24, 2010 06:00 AM | 5

**Finding Santa Claus's home at the North Pole is easy on a globe—just look for the point on top where all the lines of longitude meet. But that is just the "geographic" North Pole; there are several other definitions for the poles, all useful in different scientific or navigational contexts. Among the many north poles, let us rejoice that Santa Claus did not choose the magnetic pole for his home, for he would have to spend as much time moving as delivering presents.**

The north magnetic pole (NMP), also known as the dip pole, is the point on Earth where the planet's magnetic field points straight down into the ground. Scottish explorer James Clark Ross first located the NMP in 1831 on the Boothia Peninsula in what is now northern Canada, and with the planting of a flag claimed it for Great Britain.

But the NMP drifts from year to year as geophysical processes within Earth change. For more than 150 years after Ross's measurement its movement was gradual, generally less than 15 kilometers per year. But then, in the 1990s, it picked up speed in a big way, bolting north–northwest into the Arctic Ocean at more than 55 kilometers per year. If it keeps going it could pass the geographic north pole in a decade or so and carry on toward Siberia. But why?

One compelling explanation appears in the December 21 *Eos*, the weekly transactions of the American Geophysical Union. In their *Eos* article (subscription required), and in a longer paper published earlier in 2010 in the *Journal of Geophysical Research—Solid Earth*, Arnaud Chulliat of the Institute of Earth Physics of Paris and his colleagues venture that a twisting molten plume beneath the Arctic could be the cause:

*According to some recent models, plumes of less dense fluid form at the inner core boundary and subsequently rise within [a cylinder] whose central axis is the Earth's rotation axis. Such plumes undergo a strong helical motion due to the Earth's rapid rotation, a phenomenon also observed in laboratory experiments with water. In the core, helical plumes advect and twist the magnetic field lines, forming what scientists call "polar magnetic upwellings."*

Those upwellings, unloaded into the Arctic mantle, could produce intense patches of magnetic activity on the sort of decade-long timescales needed to explain the NMP's sudden acceleration. (The authors compare these patches to a kind of terrestrial version of sunspots.) And magnetic field measurements show dramatic shifts near the New Siberian Islands that seem to fit the bill.

"What happened under the New Siberian Islands at the core surface is that the rate of change of the magnetic field changed by a large amount during the 1990s," Chulliat says. That activity, he and his colleagues have found, could account for a large portion of the NMP's acceleration. But whether magnetic field changes under the New Siberian Islands and the speeding north magnetic pole ultimately arise from a twisted plume of fluid rising through the core remains unproved, Chulliat and his co-authors note. A resolution of the mystery will await better modeling, along with more data from satellites monitoring the Arctic's magnetic environment. The necessity of satellites, interestingly enough, is a consequence of the pole's recent movement—as the NMP drifts farther out to sea, it becomes harder and harder to reach the region with magnetometer-equipped aircraft.

<http://news.sciencemag.org/sciencenow/2010/12/a-supplement-to-stop-seizures.html>

## **A Supplement to Stop Seizures**

by Allison Bohac

***Most people know how hard it can be to stick to a diet. But for children with epilepsy, maintaining a restrictive high-fat, low-carbohydrate regimen known as the ketogenic diet is far more difficult than any weight-loss plan. Someday, however, they may be able to control seizures with a simple supplement instead, if a new finding in mice holds up in humans.***

Almost a third of epilepsy patients, many of them children, don't respond to antiseizure drugs. For reasons that are not well understood, the ketogenic diet can prevent seizures for some of these children. But it's by no means an easy fix.

Patients need to eat 80% to 90% of their daily calories as fat, usually in the form of vegetable oil or butter. Only some versions of the diet allow any carbohydrates at all, and sugary desserts are off-limits. "Eating a cookie can break the effect of the diet, resulting in a seizure," explains Karin Borges, a neurobiologist at the University of Queensland, Brisbane, in Australia.

Hoping to design a more palatable alternative to the ketogenic diet, Borges and her colleagues began experimenting with a synthetic oil often found in antiwrinkle creams and other cosmetics. The compound, called triheptanoin, is already used to treat certain metabolic disorders; researchers believe it works because it replenishes specific molecules needed to produce the energy-carrying molecule adenosine triphosphate (ATP).

Borges reasoned that these metabolites, which are also the building blocks for certain chemical messengers in the brain, might be depleted by the flurry of brain activity that occurs during a seizure. Lower ATP levels in the brain can destabilize neurons, triggering more seizures. Borges hoped that a diet supplemented with triheptanoin would replenish the brain's supply of metabolites and boost ATP production, helping to control epileptic bursts.

She and her colleagues tested this hypothesis in mice. Some of the rodents ate a normal laboratory diet, but others were fed a diet in which 35% of the calories came from triheptanoin. After 3 weeks, the researchers induced seizures in the mice using either a drug injection or electrical stimulation of the brain. It was more difficult to produce seizures in mice on the 35% triheptanoin diet, the team reports in this month's issue of *Neurobiology of Disease*. The supplement had effects similar to those of some antiseizure drugs currently on the market, says Borges.

The team also found that triheptanoin restores some of the brain's missing metabolites. But Borges cautions that there is a lot more research to do before her team knows for sure why the supplement acts as an anticonvulsant. The next step will be preparation for a clinical trial, she says, to see if what works for mice will be safe for people.

For humans, a diet composed of one-third triheptanoin adds up to almost 800 calories. Borges is hoping epilepsy patients won't need quite such a high dose, however. If the compound works for them, she says, they should be able to resume a normal diet; they would just need to add the flavorless compound to their food, possibly by mixing it into sauces and salad dressings.

Targeting metabolites specifically, says Susan Masino, a neurobiologist at Trinity College in Hartford, Connecticut, "is a new concept in epilepsy therapy." She believes that a dietary supplement like triheptanoin could make metabolic therapy more realistic for more people.

Adam Hartman, a pediatric neurologist at the Johns Hopkins University School of Medicine in Baltimore, Maryland, agrees. Borges's research, he says, establishes that putting metabolites back into the brain is a viable technique for treating epilepsy. And, because triheptanoin has been used to treat humans in the past, the outlook for conducting a clinical trial is good.

[http://www.eurekalert.org/pub\\_releases/2010-12/mgh-sdw122210.php](http://www.eurekalert.org/pub_releases/2010-12/mgh-sdw122210.php)

**Structure deep within the brain may contribute to a rich, varied social life**  
**Scientists have discovered that the amygdala, a small almond shaped structure deep within the temporal lobe, is important to a rich and varied social life among humans.**

The finding was published this week in a new study in Nature Neuroscience and is similar to previous findings in other primate species, which compared the size and complexity of social groups across those species.

"We know that primates who live in larger social groups have a larger amygdala, even when controlling for overall brain size and body size," says Lisa Feldman Barrett, PhD, of the Massachusetts General Hospital (MGH) Psychiatric Neuroimaging Research Program and a Distinguished Professor of Psychology at Northeastern University, who led the study. "We considered a single primate species, humans, and found that the amygdala volume positively correlated with the size and complexity of social networks in adult humans."

The researchers also performed an exploratory analysis of all the subcortical structures within the brain and found no compelling evidence of a similar relationship between any other subcortical structure and the social life of humans. The volume of the amygdala was not related to other social variables in the life of humans such as life support or social satisfaction.

"This link between amygdala size and social network size and complexity was observed for both older and younger individuals and for both men and women," says Bradford C. Dickerson, MD, of the MGH Department of Neurology and the Martinos Center for Biomedical Research. "This link was specific to the amygdala, because social network size and complexity were not associated with the size of other brain structures." Dickerson is an associate professor of Neurology at Harvard Medical School, and co-led the study with Dr. Barrett.

The researchers asked 58 participants to report information about the size and the complexity of their social networks by completing standard questionnaires that measured the total number of regular social contacts that each participant maintained, as well the number of different groups to which these contacts belonged. Participants, ranging in age from 19 to 83 years, also received a magnetic resonance imaging brain scan to gather information about the structure of various brain structures, including the volume of the amygdala.

A member of the the Martinos Center at MGH, Barrett also notes that the results of the study were consistent with the "social brain hypothesis," which suggests that the human amygdala might have evolved partially to deal with an increasingly complex social life. "Further research is in progress to try to understand more about how the amygdala and other brain regions are involved in social behavior in humans," she says. "We and other researchers are also trying to understand how abnormalities in these brain regions may impair social behavior in neurologic and psychiatric disorders."

*Co-Authors of the Nature Neuroscience paper are Kevin C. Bickart, Boston University School of Medicine; and Christopher I. Wright, MD, PhD, and Rebecca J. Dautoff of the MGH Psychiatric Neuroimaging Research Program and the Martinos Center. The study was supported by grants from the US National Institutes of Health and the US National Institute on Aging.*

[http://www.eurekalert.org/pub\\_releases/2010-12/giot-gtt122310.php](http://www.eurekalert.org/pub_releases/2010-12/giot-gtt122310.php)

**Georgia Tech team helps decode newly sequenced strawberry genome**  
**An international research consortium has sequenced the genome of the woodland strawberry, according to a study published in the Dec. 26 advance online edition of the journal Nature Genetics.**

The development is expected to unlock possibilities for breeding tastier, hardier varieties of the berry and other crops in its family.

"We've created the strawberry parts list," said the consortium's leader Kevin Folta, an associate professor with the University of Florida's Institute of Food and Agricultural Sciences. "For every organism on the planet, if you're going to try to do any advanced science or use molecular-assisted breeding, a parts list is really helpful. In the old days, we had to go out and figure out what the parts were. Now we know the components that make up the strawberry plant."

From a genetic standpoint, the woodland strawberry, formally known as *Fragaria vesca*, is similar to the cultivated strawberry but less complex, making it easier for scientists to study. The 14-chromosome woodland strawberry has one of the smallest genomes of economically significant plants, but still contains approximately 240 million base pairs.

The consortium of 75 researchers from 38 institutions that sequenced the genome included two Georgia Tech researchers. They are Mark Borodovsky, a Regents professor with a joint appointment in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University and the Georgia Tech

School of Computational Science and Engineering, and Paul Burns, who worked on the project as a bioinformatics Ph.D. student.

Once the consortium uncovered the genomic sequence of the woodland strawberry, Borodovsky and Burns led the efforts in identifying protein-coding genes in the sequence. Using a newly developed pattern recognition program called GeneMark.hmm-ES+, Borodovsky and Burns identified 34,809 genes, of which 55 percent were assigned to gene families.

The GeneMark.hmm-ES+ program iteratively identified the correct algorithm parameters from the DNA sequence and transcriptome data. The program used a probabilistic model called the Hidden Markov Model to pinpoint the boundaries between coding sequences -- called exons -- and non-coding sequences, which could be either introns or intergenic regions.

In identifying the genes, prediction and training steps were repeated, each time detecting a larger set of true coding and non-coding sequences used to further improve the model employed in statistical pattern recognition. When the new sequence breakdown coincided with the previous one, the researchers recorded their final set of predicted genes.

"GeneMark.hmm-ES+ is a hybrid program that uses both DNA and RNA sequences to predict protein-coding genes," said Borodovsky, who is also director of Georgia Tech's Center for Bioinformatics and Computational Genomics.

Borodovsky developed the first version of GeneMark in 1993. In 1995, this program was used to find genes in the first completely sequenced genomes of bacteria and archaea. The research team then developed self-training versions of the gene finding program for prokaryotic (organisms that lack a cell nucleus) and eukaryotic (organisms that contain a cell nucleus) genomes in 2001 and 2005, respectively. Development of these programs has been supported by the National Institutes of Health since 1993.

Most recently, Borodovsky's team predicted genes in the genomes of the green alga *Chlorella variabilis* NC64A and the mushroom *Coprinopsis cinerea*, with reports published in 2010 in the journals *The Plant Cell* and *Proceedings of the National Academy of Sciences*, respectively.

"Our approach to gene prediction in the strawberry genome proved highly effective, with 90 percent of the genes predicted by the hybrid gene model supported by transcript-based evidence," added Borodovsky.

Further analysis of the woodland strawberry genome revealed genes involved in key biological processes, such as flavor production, flowering and response to disease. Additional examination also revealed a core set of signal transduction elements shared between the strawberry and other plants.

The woodland strawberry is a member of the Rosaceae family, which consists of more than 100 genera and 3,000 species. This large family includes many economically important and popular fruit, nut, ornamental and woody crops, including the cultivated strawberry, almond, apple, peach, cherry, raspberry and rose.

In the long term, breeders will be able to use the information to create plants that can be grown with less environmental impact, better nutritional profiles and larger yields.

"The wealth of genetic information collected by this strawberry genome sequencing project will help spur the next wave of research into the improvement of strawberry and other fruit crops," added Borodovsky.

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[http://www.eurekalert.org/pub\\_releases/2010-12/ps-ot122110.php](http://www.eurekalert.org/pub_releases/2010-12/ps-ot122110.php)

### **'Food of the gods' genome sequence could make finest chocolate better**

***The production of high quality chocolate, and the farmers who grow it, will benefit from the recent sequencing and assembly of the chocolate tree genome, according to an international team led by Claire Lanaud of CIRAD, France, with Mark Guiltinan of Penn State, and including scientists from 18 other institutions.***

The team sequenced the DNA of a variety of *Theobroma cacao*, considered to produce the world's finest chocolate. The Maya domesticated this variety of *Theobroma cacao*, Criollo, about 3,000 years ago in Central America, and it is one of the oldest domesticated tree crops. Today, many growers prefer to grow hybrid cacao trees that produce chocolate of lower quality but are more resistant to disease.

"Fine cocoa production is estimated to be less than 5 percent of the world cocoa production because of low productivity and disease susceptibility," said Guiltinan, professor of plant molecular biology.

The researchers report in the current issue of *Nature Genetics* "consumers have shown an increased interest for high-quality chocolate made with cocoa of good quality and for dark chocolate, containing a higher percentage of cocoa, while also taking into account environmental and ethical criteria for cocoa production."

Currently, most cacao farmers earn about \$2 per day, but producers of fine cacao earn more. Increasing the productivity and ease of growing cacao can help to develop a sustainable cacao economy. The trees are now

also seen as an environmentally beneficial crop because they grow best under forest shade, allowing for land rehabilitation and enriched biodiversity.

The team's work identified a variety of gene families that may have future impact on improving cacao trees and fruit either by enhancing their attributes or providing protection from fungal diseases and insects that effect cacao trees.

"Our analysis of the Criollo genome has uncovered the genetic basis of pathways leading to the most important quality traits of chocolate -- oil, flavonoid and terpene biosynthesis," said Siela Maximova, associate professor of horticulture, Penn State, and a member of the research team. "It has also led to the discovery of hundreds of genes potentially involved in pathogen resistance, all of which can be used to accelerate the development of elite varieties of cacao in the future."

Because the Criollo trees are self-pollinating, they are generally highly homozygous, possessing two identical forms of each gene, making this particular variety a good choice for accurate genome assembly.

The researchers assembled 84 percent of the genome identifying 28,798 genes that code for proteins. They assigned 88 percent or 23,529 of these protein-coding genes to one of the 10 chromosomes in the Criollo cacao tree. They also looked at microRNAs, short noncoding RNAs that regulate genes, and found that microRNAs in Criollo are probably major regulators of gene expression.

"Interestingly, only 20 percent of the genome was made up of transposable elements, one of the natural pathways through which genetic sequences change," said Guiltinan "They do this by moving around the chromosomes, changing the order of the genetic material. Smaller amounts of transposons than found in other plant species could lead to slower evolution of the chocolate plant, which was shown to have a relatively simple evolutionary history in terms of genome structure."

Guiltinan and his colleagues are interested in specific gene families that could link to specific cocoa qualities or disease resistance. They hope that mapping these gene families will lead to a source of genes directly involved in variations in the plant that are useful for acceleration of plant breeding programs.

The researchers identified two types of disease resistance genes in the Criollo genome. They compared these to previously identified regions on the chromosomes that correlate with disease resistance -- QTLs -- and found that there was a correlation between many the resistance genes' QTL locations. The team suggests that a functional genomics approach, one that looks at what the genes do, is needed to confirm potential disease resistant genes in the Criollo genome.

Hidden in the genome the researchers also found genes that code for the production of cocoa butter, a substance highly prized in chocolate making, confectionary, pharmaceuticals and cosmetics. Most cocoa beans are already about 50 percent fat, but these 84 genes control not only the amounts but quality of the cocoa butter.

Other genes were found that influence the production of flavonoids, natural antioxidants and terpenoids, hormones, pigments and aromas. Altering the genes for these chemicals might produce chocolate with better flavors, aromas and even healthier chocolate.

*Penn State researchers involved in this study include Guiltinan and Maximova; Yufan Zhang and Zi Shi, graduate students, plant biology; Stephen Schuster, Department of Biochemistry and Molecular Biology; John E. Carlson, School of Forest Resources and M.J. Axtell and Z. Ma, Department of Biology.*

*Other researchers involved were from CIRAD; Institut National de la Recherche Agronomique UMR; Genoscope; Centre National de la Recherche Scientifique; Centre National de Genotypage; Universite d'Evry; INRA-CNRS LIPM Laboratoire des Interactions Plantes Micro-organismes; Universite de Perpignan; Unite de Biometrie et d'Intelligence Artificielle; Institut des Sciences du Vegetal; and Chocolaterie Valrhona, all in France.*

*Also included are researchers from the University of Arizona; Cold Spring Harbor Laboratory; Centre National de la Recherche Agronomique, Ivory Coast; CEPLAC, Brazil; and Centro Nacional de Biotecnologia Agricola, Instituto de Estudios Avanzados, Venezuela.*

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*The Theobroma cacao genome sequences are deposited in the EMB:/Genbank/DDBJ databases under accession numbers CACC01000001-CACC01025912. A genome browser and further information on the project are available from <http://cocoagendb.cirad.fr/gbrowse> and <http://cocoagendb.cirad.fr>.*