More is merrier for wireless power supply

* 10:00 14 February 2010 by **Nic Fleming**

Using magnetic induction to send electricity to devices is more efficient when more than one machine is involved. The notion of transmitting power over the air is at least 100 years old, with methods from high-powered microwaves to focused beams of infrared being tested.

But researchers at the Massachusetts Institute of Technology (MIT), led by physicist Marin Soljacic, think using magnetic fields to induce a current in a distant device is the most promising approach. They tune the transmitter and receiver to magnetically resonate at the same frequency to maximise efficiency. Waves carry energy most effectively between objects that resonate at the same frequency, an effect at work when a singer smashes a nearby glass with the right note.

Two's better than one

In 2007, Soljacic's team reported they could light a 60-watt bulb from across a room.

Now the they have shown it is possible to power two devices wirelessly when they are placed on either side of a single 1–square-metre coil. A network analyser measured the efficiency of the power transfer, while the researchers varied the distance between the source and receivers from 1.6 metres to 2.7 metres.

The researchers found that power transfer was 10 per cent more efficient with two devices receiving rather than one, regardless of how efficient the transfer was to begin with. Their models suggested that efficiency would be even greater with more devices. Because the efficiency boost is always roughly 10 percentage points, the relative improvement is greatest when a lone device is joined by another, says André Kurs, lead author of a paper on the experiments.

Room coverage

That makes it possible to power a collection of devices with poor individual links, perhaps because they are scattered across a room far from the coil. "We could have reasonably good efficiency over a room-sized area from a coil embedded in ceiling or a wall in order to power multiple gadgets or devices," said Kurs. The efficiency increases because more of the broadcasting coil's field falls on receptive receivers.

"This is a promising road to full wireless connectivity, not just for signals but also for power," says electrical engineer Luk Arnaut of Imperial College London. "However, the efficiency of the system rapidly deteriorates with increasing distance," he adds, explaining that specialised antennae will need to be developed to counter that.

The MIT researchers have set up a spin off company called WiTricity Corporation, joining electronics firms such as Sony in trying to commercialise wireless electricity transfer.

Journal reference: Applied Physics Letters, DOI:10.1063/1.3284651

Bacteria-killing proteins cover blood type blind spot

A set of proteins found in our intestines can recognize and kill bacteria that have human blood type molecules on their surfaces, scientists at Emory University School of Medicine have discovered.

The results were published online Feb. 14 and are scheduled to appear in the journal Nature Medicine.

Many immune cells have receptors that respond to molecules on the surfaces of bacteria, but these proteins are different because they recognize structures found on our own cells, says senior author Richard D. Cummings, PhD, professor and chair of the Department of Biochemistry. "It's like having a platoon in an army whose sole purpose is to track down enemy soldiers that are wearing the home country's uniforms."

Blood type comes from differences in sugar molecules attached to proteins on red blood cells. If incompatible blood types are mixed, the antibodies from one person will make red blood cells from the other person clump together, with devastating results in an emergency. But someone's immune system usually doesn't make antibodies to the sugar molecules on his or her own red blood cells. That creates a potential blind spot that bacteria could exploit.

For example, a strain of E. coli (O86) has molecules on its surface like those in humans with blood type B. People with blood type B are unable to produce antibodies against E. coli O86. Although O86 is known to infect birds, it's not a major danger like other types of E. coli, some of which can cause severe diarrhea.

Cummings and his colleagues wanted to know why more bacteria haven't adopted the tactics of E. coli O86 to get around the immune system. Searching for proteins that could bind to the sugar molecules characteristic of blood types A and B, graduate students Sean Stowell, PhD, and Connie Arthur identified proteins called galectin-4 and galectin-8.

"These proteins are separate from antibodies and other parts of the immune system," Cummings says. "They kill bacteria like E. coli O86 all by themselves within a couple of minutes."

When E. coli O86 is exposed to these proteins and viewed by electron microscopy, "it looks as if somebody is tearing away at their outer membranes," he adds.

However, galectins-4 and -8 did not kill human red blood cells expressing blood group antigens. High levels of lactose (milk sugar) can inhibit the lethal activity of these galectins, whereas sucrose (cane sugar) does not.

"This raises the question of whether there are dietary effects, as from milk sugars or other dietary polysaccharides, that might inhibit activity of these galectins on intestinal microbes and their proliferation and colonization," Cummings says.

Cummings notes the unique properties of galectins-4 and -8 may provide an explanation for why the human population has such a diversity of sugar molecules on blood cells. The diversity may ensure that some part of the population might be able to fend off a bacterial infection. For example, ABO blood type seems to affect susceptibility to Helicobacter pylori, a bacterium linked to ulcers.

Galectins were thought to have evolved long before "adaptive immunity," the part of vertebrates' immune systems that is responsible for producing a variety of antibodies. Galectins may have allowed the generation of a diverse group of blood type sugar molecules in human tissues as a safe set of molecules to evolve because immunity is backstopped by galectins, Cummings says.

Galectins-4 and-8 were also able to kill another variety of E. coli that display a sugar molecule found on many mammalian cells, although more protein was needed. That leads to a question Cummings and his colleagues are investigating now: What else do galectins recognize, and how does that constrain the kinds of bacteria that can live in our intestines? In addition, it may now be possible, given these results, to engineer molecular changes in these galectins to allow them to kill other types of pathogenic bacteria that display other types of sugar molecules on their surface. Such developments could lead to new types of antibiotics for pathogenic microbes.

The research was supported by the National Institute of General Medical Sciences of the National Institutes of Health and the Consortium for Functional Glycomics and also involved key contributions from Marcelo Dias-Baruffi, PhD, and colleagues at the Universidade de São Paolo in Ribeirão Preto, Brazil.

Reference: *S.R. Stowell et al. Innate immune lectins kill bacteria expressing blood group antigen. Nat. Med. 16, page numbers (2010).*

Developing guidelines for better reporting of health research

A paper published in this week's issue of PLoS Medicine provides a substantial new resource for the developers of guidelines of the reporting of health research. The authors of the paper have been key in the development of many of the most important health research guidelines published over the past few years, including the CONSORT guidelines for clinical trials and the PRISMA guidelines for systematic reviews.

The accurate reporting of a study is key to the understanding of the importance of the study. Before the development of CONSORT, for example, there was no consensus on what must be reported in order for a reader to accurately assess the validity of a trial. Hence, even such important items such as method of randomization and the primary outcome of the trial were routinely left out, leading to studies being reported in a misleading fashion.

The authors of this report are part of a larger group of experts who have for many years been advocating for, and producing guidelines aimed at the improvement of reporting of health research. The importance of these guidelines is now increasingly recognized by the wider research community, and, moreover, they are increasingly required by journals. In addition to individual guidelines this group has also spearheaded the development of an overarching network, the EQUATOR Network, which contains most of the currently developed guidelines - http://www.equator-network.org/. This paper represents a further effort to promote better reporting" As the authors note "If reporting guidelines are to be useful and more widely disseminated, they need to be developed using robust and widely accepted methodologies.

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Competing interests: *DM, KFS, IS, and DGA are members of the EQUATOR Network. DM, KFS, and DGA are members of the CONSORT executive. DM and DGA are members of the PRISMA executive. DM is on the Editorial Board of PLoS Medicine.*

Citation: *Moher D, Schulz KF, Simera I, Altman DG (2010) Guidance for Developers of Health Research Reporting Guidelines. PLoS Med 7(2): e1000217.doi:10.1371/journal.pmed.1000217.*

Genetic code 2.0: Life gets a new operating system

* 18:00 14 February 2010 **by Linda Geddes**

A new way of using the genetic code has been created, allowing proteins to be made with properties that have never been seen in the natural world. The breakthrough could eventually lead to the creation of new or "improved" life forms incorporating these new materials into their tissue.

In all existing life forms, the four "letters" of the genetic code, called nucleotides, are read in triplets, so that every three nucleotides encode a single amino acid.

Not any more. Jason Chin at the University of Cambridge and his colleagues have now redesigned the cell's machinery so that it reads the genetic code in quadruplets.

In the genetic code that life has used up to now, there are 64 possible triplet combinations of the four nucleotide letters; these genetic "words" are called codons. Each codon either codes for an amino acid or tells the cell to stop making a protein chain. Now Chin's team have created 256 blank four-letter codons that can be assigned to amino acids that don't even exist yet.

Fundamental redesign

To achieve this, the team had to redesign three pieces of the cellular machinery that make proteins.

But they didn't stop there. The team went on to prove their new genetic code works by assigning two "unnatural" amino acids to their quadruplet codons, and incorporated them into a protein chain.

"It's the beginning of a parallel genetic code," says Chin.

Stronger bonds

What's more, they've shown that these amino acids can react with each other to form a different kind of chemical bond to those which usually hold proteins together in their three-dimensional shape.

The normal kind of bonds – disulphide bonds – can be broken by changes in heat and acidity, causing proteins to lose their 3D structure. This, for instance, is why egg whites change colour and texture when cooked: as the albumen in the whites loses its structure, its physical appearance is transformed.

But the bonds created between Chin's new amino acids are stronger – and so could allow proteins to work in a much wider range of environments. This could help make drugs that can be taken orally without being destroyed by the acids in the digestive tract, for instance.

But that's just the beginning. In the longer term it might be possible to create cells that produce entirely new polymers, such as plastic-like materials. Organisms made of these cells could incorporate the stronger polymers and become stronger or more adaptable as a result.

"It's a very impressive advance that opens up new theoretical horizons in synthetic biology," says genomics pioneer Craig Venter, who heads his own institute in Rockville, Maryland, and is currently trying to create a synthetic organism from scratch. *Journal reference: Nature, DOI: 10.1038/nature08817*

Really?

The Claim: Counting Sheep Helps You Fall Asleep

By ANAHAD O'CONNOR

THE FACTS The reason people count sheep, as opposed to bluebirds or sailboats, is uncertain; some authorities think it may have to do with a tallying system devised by shepherds in ancient Britain. But there is no question that the phrase has entered the language. And its meaning is clear enough - the sheer monotony of the task is meant to lull you to sleep.

But does it work? Scientists at Oxford University put it to the test. In their study, which appeared in the journal Behavior Research and Therapy, two sleep researchers recruited insomniacs and split them into groups. Then they monitored them as they tried different techniques for falling asleep on various nights.

What they found was that subjects took slightly longer to fall asleep on nights they were instructed to distract themselves by counting sheep or were given no instructions at all. But when they were told to imagine a relaxing scene - a beach, for example - they fell asleep an average of 20 minutes sooner than they did on other nights. Counting sheep, the scientists suggested, may simply be too boring to do for very long, while images of a soothing shoreline or tranquil stream are engrossing enough to concentrate on.

In other studies at Oxford, scientists compared "good" sleepers with insomniacs and found distinct differences in their pre-sleep thoughts. Insomniacs pictured less scenery of any kind and had more thoughts of unpleasant images, worries, noises in the environment, "intimate relationships" and things they had done during the day.

THE BOTTOM LINE Don't count sheep; instead, try picturing relaxing images.

Pliable power pack will let gadgets feed on your body

* 15 February 2010 **by MacGregor Campbell**

SHEETS of material that produce voltage when flexed could generate power from the motion of the human body. Previous materials were either too rigid or too inefficient to be practical as pliable power generators. Now two research teams have solved the problem using different approaches. The materials could allow future medical implants to harvest their own power, by using the pulsing of arteries, for example.

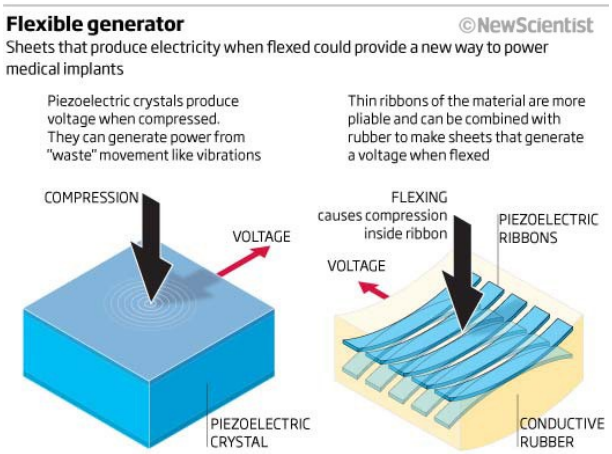
Yi Qi and Michael McAlpine of Princeton University developed a way to soften up the usually inflexible crystal lead-zirconate-titanate (PZT), which is one of the most efficient piezoelectric materials known.

"People thought, 'this is a crystal'; they never thought about whether they could make it flexible," says McAlpine. But he and Qi found that when an extremely thin film of the ceramic is grown on a solid substrate and cut into strips about 5 micrometres thick, the resulting material can flex (see diagram).

These "nanoribbons" are like fibre-optic cable made using glass, says McAlpine. Being long and thin, they can still bend despite being made of a material that is rigid in bulk.

The strips were attached to conducting silicone rubber to produce a flexible sheet that converts motion to electricity about half as well as traditional, rigid PZT (Nano Letters, DOI: 10.1021/nl903377u).

In contrast, Chieh Chang and Liwei Lin of the University of California at Berkeley created fibres from a piezoelectric polymer called PVDF. The polymer is usually made in sheets, but the researchers spun it into fibres by drawing the molten material through a nozzle using an electric field.



This technique usually results in a fibre inside which the charged domains responsible for the material's useful properties are randomly oriented, leading them to cancel out one another's output. The Berkeley team used a strong electric field and the mechanical stress of the spinning process to line up those domains and ensure they work in unison.

When more than 40 samples were tested the fibres proved capable of converting 12.5 per cent of the mechanical energy used to deform them into electricity. Some recovered 20 per cent (Nano Letters, DOI: 10.1021/nl9040719). Lin says this makes them competitive with a conventional film of rigid PZT.

"Using flexible materials will open up a new field of mechanical energy harvesting," says Xudong Wang at the University of Wisconsin, Madison, who says "waste" movement is often overlooked as an energy source.

McAlpine says flexible piezomaterials of either kind could be used to make motion-powered generators to extend the battery life of medical devices like pacemakers. "You could even eliminate the battery altogether." he says.

A gene for Alzheimer's makes you smarter

* 15 February 2010 **by Ewen Callaway**

A GENE variant that ups your risk of developing Alzheimer's disease in old age may not be all bad. It seems that young people with the variant tend to be smarter, more educated and have better memories than their peers.

The discovery may improve the variant's negative image (see "Yes or no"). It also suggests why the variant is common despite its debilitating effects in old age. Carriers of the variant may have an advantage earlier in life, allowing them to reproduce and pass on the variant before its negative effects kick in. "From an evolutionary perspective it makes sense," says Duke Han at Rush University Medical Center in Chicago.

The "allele" in question is epsilon 4, a version of the apolipoprotein E gene (APOE). Having one copy increases the risk of developing Alzheimer's at least fourfold compared with people who have other forms of the gene. A person with two copies has up to 20 times the risk.

One big clue that epsilon 4 might be beneficial emerged several years ago, when Han's team scanned the APOE genes of 78 American soldiers. All had suffered traumatic brain injuries, many while serving in Iraq. Sixteen had at least one copy of epsilon 4. Han's team expected to find that these carriers would be in worse cognitive shape than their counterparts with different versions of APOE, given previous studies that showed elderly people with epsilon 4 fare worse after head injury. But the opposite was true: soldiers with the epsilon 4 allele had better memory and attention spans (Journal of Neurology, Neurosurgery & Psychiatry, DOI: 10.1136/jnnp.2006.108183).

It wasn't the first study to suggest that epsilon 4 may be beneficial to the young. Back in 2000, researchers showed that young women with epsilon 4 have IQs a few points higher than those with no copies of the variant and score 7 points higher on the non-verbal portion of a common intelligence test (Neuroscience Letters, vol 294, p 179). Then in the Czech Republic in 2001, researchers showed that 87 per cent of epsilon 4 carriers go on to university, compared with 55 per cent of people with another version of APOE. The last group were also more likely to drop out of school (Neuropsychobiology, DOI: 10.1159/000054890).

More recently, Jenny Rusted of the University of Sussex, UK, and Natalie Marchant at the University of California, Berkeley, have uncovered still more benefits for young people carrying epsilon 4. Those aged between 18 and 30 with the gene variant excelled at tasks requiring the frontal lobe, a brain region involved in higher cognitive skills. In particular, epsilon 4 carriers did better in a card game that asked them to remember a future plan while busy with another task (Neuropsychopharmacology, DOI: 10.1038/npp.2009.214).

Rusted suggests that epsilon 4 helps people focus on important information. But recalling something also requires you to tune out the irrelevant bits, an ability known to decline with age.

Perhaps, Rusted says, without this second capability, epsilon 4's benefits fall by the wayside. Why it has a negative effect in old age, however, is still a mystery, although a study carried out by Clare MacKay at the University of Oxford in 2009 offers a tentative, hypothesis.

Her team asked 20 to 35-year-olds to remember which pictures of animals or landscapes they had seen before, while having their brains scanned with functional MRI. It was an easy task and all performed equally well. But a brain region critical to memory lit up more strongly in epsilon 4 carriers than in the others, raising the intriguing possibility that carriers' brains get overworked in early life, only to be worn out by the time they hit old age. MacKay wouldn't go that far, but she says: "It's possible that your brain is having to work harder when it's younger and this may have consequences for later life."

Yes or No to knowing if you have epsilon 4?

When DNA co-discoverer James Watson published his genome in 2007, he left one tiny bit out: the piece that would have told him which version of the APOE gene he has. He opted not to know whether he was carrying the epsilon 4 version, which can vastly increase the odds of developing Alzheimer's disease.

He's not the only one to make an exception for APOE: Harvard University psychologist Steven Pinker, one of several high-profile scientists planning to make his genome freely available as part of the Personal Genome Project, will follow Watson's lead and keep his APOE sequence a mystery.

In contrast, genome pioneer Craig Venter has let the world know that he has one copy of epsilon 4, which also increases the odds of developing heart disease - and has started taking a cholesterol-lowering drug that he hopes may also delay Alzheimer's.

Scientific celebrities aren't the only ones who agonise over their APOE status. Anyone who has forked out a few hundred dollars to have their genome scanned can decide whether to find out if their APOE gene puts them at increased risk of Alzheimer's.

Knowing your status may not be all bad, says Robert Green of Boston University in Massachusetts, who over two years monitored how people reacted to finding out which version of the gene they have (The New England Journal of Medicine, vol 361, p 245). "By and large there were no catastrophic reactions," he says. The only people whose mood changed much were those relieved to discover they didn't have the risky variant.

If epsilon 4 does improve cognition in young adults (see main story) does that strengthen the case for knowing whether you carry that version?

Clare MacKay, who studies the effect of epsilon 4 on cognition at Oxford University, thinks not. "I wouldn't want to know whether I've got one and I certainly wouldn't want other people to know." Her lab is forbidden from telling the volunteers their APOE status. "It will only be a good idea to know your APOE genotype when there's something we can do about it," she says.

Space rock contains organic feast

By Doreen Walton Science reporter, BBC News

Scientists say that a meteorite that crashed into Earth 40 years ago contains millions of different carbon-containing, or organic, molecules. Although they are not a sign of life, such organic compounds are life's building blocks, and are a sign of conditions in the early Solar System.

It is thought the Murchison meteorite could even be older than the Sun.

The results of the meteorite study are published in the Proceedings of the National Academy of Sciences.

The Murchison meteorite came down in Australia in 1969

"We are really excited. When I first studied it and saw the complexity I was so amazed," said Philippe Schmitt-Kopplin, lead researcher on the study from the Institute for Ecological Chemistry in Neuherberg, Germany.

"Having this information means you can tell what was happening during the birth of the Solar System," Dr Schmitt-Kopplin told BBC News. "Meteorites are like some kind of fossil. When you try to understand them you are looking back in time," he explained.

The researchers says the identification of many different chemicals shows the primordial Solar System probably had a higher molecular diversity than Earth.

The Murchison meteorite landed in a town of that name in Australia in 1969. It has been examined before by scientists looking for specific compounds but this is the first non-targeted analysis and has confirmed a huge variety of carbon-based chemicals.

A study using high resolution analytical tools including spectroscopy allowed the team to identify 14,000 different compounds.

The scientists extrapolated the number on the basis of previous analyses done on natural organic matter.

The ultra-high-resolution mass spectrometry used shows only a fraction of the compounds that exist in the material being analysed, in this case the meteorite.

However the scientists say the prior studies allow them to make a good estimate of the total number of compounds. "We were very conservative in our calculations and interpolation," said Dr Schmitt-Kopplin.

"We have to crush a few milligrams from the core of the meteorite to enable the extractions with solvents and thus we only see the extractable fraction."

Burning question

Scientists believe the Murchison meteorite could have originated before the Sun was formed, 4.65 billion years ago. The researchers say it probably passed through primordial clouds in the early Solar System, picking up organic chemicals.

Dr Schmitt-Kopplin hopes the findings might contribute to the debate over how life on Earth originated.

"I guess many people working in these fields with access to this knowledge will have some further hypothesis and will possibly be having some of their hypotheses confirmed."

"Where did we come from and what happened before? We all have that question inside us."

The team is also analysing other meteorites but say Murchison is probably the most complex they have studied.

Scientists transplant nose of mosquito, advance fight against malaria

Scientists at Vanderbilt and Yale universities have successfully transplanted most of the "nose" of the mosquito that spreads malaria into frog eggs and fruit flies and are employing these surrogates to combat the spread of the deadly and debilitating disease that afflicts 500 million people. The research is described in two complimentary papers, one published this week in the early online edition of the Proceedings of the National Academy of Sciences and the other which appeared online Feb. 3 in the journal Nature.

The mosquito's "nose" is centered in its antennae, which are filled with nerve cells covered with special "odorant receptors" that react to different chemical compounds. The insect ORs are comparable to analogous receptors in the human nose and taste buds on the tongue.

"We've successfully expressed about 80 percent of the Anopheles mosquito's odorant receptors in frog's eggs and in the fruit fly antennae," says Laurence Zwiebel, professor of biological sciences at Vanderbilt, whose lab performed the frog egg transplantation. The fruit-fly (Drosophila melanogaster) work was done in the laboratory of John Carlson, Eugene Higgins Professor of Molecular, Cellular and Developmental Biology at Yale.

Both accomplishments are part of a five-year project supported by the Grand Challenges in Global Health Initiative funded by the Foundation for NIH through a grant from the Bill & Melinda Gates Foundation with the goal of producing novel ways to inhibit the spread of malaria. Scientists from the Wageningen University in the Netherlands, the African Insect Science for Food and Health Institute in Kenya, Ifakara Health Institute in Tanzania and the Medical Research Council Laboratories in the Gambia are also participating in the project.

Previously, scientists have used frog eggs to study the olfactory receptors of moths, honeybees and fruit flies. DNA that encodes insect receptors are injected into a frog egg and given sufficient time to produce and localize proteins. As a result, the surface of the egg is covered with the mosquito odorant receptors. An engineered egg is placed in a voltage clamp system and an odorant is dissolved in the buffer solution in which the egg is floating. If the mosquito receptors react to the compound, the electrical properties of the egg change in a measurable fashion.

"The frog egg system is relatively rapid, highly sensitive and allows us to do very precise measurements of odorant response," says Guirong Wang, a senior research associate in the Zwiebel lab who was the lead author on the PNAS study and carried out several thousand egg/odorant recordings. "However, we call this a medium throughput system because, while it is relatively quick to set up, we have to make the odorant solutions by hand, which goes relatively slowly."

By comparison, Yale's Drosophila system is a somewhat lower throughput system because it takes about three months to engineer a fruit fly with a mosquito odorant receptor in its antennae. The system, originally developed in the Carlson lab, uses mutant flies that are missing an odor receptor. Allison Carey, a graduate student in the Yale lab, systematically inserted mosquito genes into fruit flies one at a time so that a mosquito odorant receptor was expressed in place of the missing receptor. Although the method is slightly slower than the frog egg approach, it has some distinct advantages: Most notably it responds to volatilized odorants so it works with compounds that don't dissolve readily in water. It is also effective in detecting chemicals that inhibit receptors rather than exciting them.

"Both teams used the same set of 72 Anopheles odorant receptors and tested them using the same panel of 110 odorants," says Wang. The Vanderbilt team got responses from 37 of the odorant receptors in the frog eggs

while testing 6,300 odorant-receptor combinations. "The results of the two systems were quite similar. There were only a few small differences."

Both studies found that most mosquito receptors are "generalists" that react to a number of different odors while a few are "specialists" that respond to a single or small number of odors. In some cases, the researchers found that a single odorant triggers several receptors while in other cases receptors are specifically tuned to unique compounds. In particular, they found 27 Anopheles receptors that respond strongly to compounds in human sweat.

"We're now screening for compounds that interact with these receptors. We call those that do BDOCs (behaviorally disruptive olfactory compounds)," Zwiebel says. "Compounds that excite some of these receptors could help lure mosquitoes into traps or repel them away from people while others that block receptor activity may help mask people. Ultimately we are looking for cocktails of multiple compounds that demonstrate activity in the field."

The project has already developed and patented a blend of BDOCs that is more attractive to mosquitoes than humans and has also identified several repellant BDOCs. It is currently in product development discussions with several private sector companies.

Botulinum toxin injection may help prevent some types of migraine pain

A preliminary study suggests the same type of botulinum injection used for cosmetic purposes may be associated with reduced frequency of migraine headaches that are described as crushing, vicelike or eye-popping (ocular), but not pain that is experienced as a buildup of pressure inside the head, according to a report in the February issue of Archives of Dermatology, one of the JAMA/Archives journals.

Migraine headaches affect approximately 28 million Americans, causing pain that is often debilitating, according to background information in the article. Researchers conducting clinical trials on botulinum toxin type A to treat facial lines recognized a correlation between injections and the alleviation of migraine symptoms. "The initial promise of a new prophylactic [preventive] therapy for migraines was met by the challenge of replication of these results," as subsequent studies have failed to demonstrate botulinum was more effective than placebo, the authors write. "Researchers have searched for patient characteristics that may predict a favorable treatment response."

Christine C. Kim, M.D., then of SkinCare Physicians, Chestnut Hill, Mass., and now in private practice in Encino, Calif., and colleagues studied 18 patients (average age 50.9) who had already received or were planning to receive botulinum injections for cosmetic purposes but also reported having migraines. Of those, 10 reported imploding headaches - described by adjectives like crushing and vice-like - or ocular headaches, reported to feel like an eye is popping out or that someone is pushing a finger into an eye. Nine patients had exploding headaches, described as feeling like one's head is going to explode or split, or that pressure is building up. Some patients had more than one type.

Three months after treatment, 13 patients had responded to the treatment with a reduction in migraine pain, including 10 who had imploding or ocular headaches and three who had exploding headaches. All six of the patients who did not respond had exploding headaches.

Among all participants who responded to treatment, migraine frequency was reduced from an average of 6.8 days per month to an average of 0.7 days per month. Patients with exploding headaches experienced an average reduction in migraine frequency of 11.4 to 9.4 days per month, whereas frequency in participants with imploding or ocular headaches reduced from an average of 7.1 days per month to 0.6 days per month.

Botulinum produces muscle paralysis, but this alone does not explain how it may prevent migraine pain, the authors note. Research indicates that it may affect the way pain signals travel through the nervous system, block pain receptors or reduce inflammation.

"These preliminary data are intriguing, and our results provide support for the hypothesis that patients with migraine that is characterized by imploding and ocular headaches are more responsive to botulinum toxin type A than those with migraine characterized by exploding headaches," the authors write. "Our findings invite consideration of using botulinum toxin type A injections to prevent migraine headaches and may promote the role of the dermatologist in the treatment of patients with migraine. However, well-controlled trials need to be conducted to confirm these findings."

(Arch Dermatol. 2010;146[2]:159-163. Available pre-embargo to the media at www.jamamedia.org.)
Editor's Note: This study was supported in part by a grant from Allergan Inc. and National Institutes of Health grants. Co-author Dr. Burstein serves as a consultant to Allergan Inc. and receives honoraria for lectures and grants for clinical and animal research. Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

Anti-ageing cream as good as drug at reducing wrinkles

* 15:07 15 February 2010 **by Linda Geddes**

The cosmetics industry could be on the brink of a much-needed facelift. For the first time, an anti-wrinkle cosmetic has been compared with the gold-standard prescription drug for skin ageing – and appears to be just as effective at reducing wrinkle depth.

As well as being good news for people who want to look younger for longer, the result – from US-based researchers at the firm Procter & Gamble – could up the pressure on cosmetics companies to offer proof of the claims they make about their products. Until now, such proof has been thin on the ground.

"I think these studies will raise the bar, because they show that you can trial these products in the same way that you trial a drug, and the cosmetics industry has never had to do that before," says Christopher Griffiths of the University of Manchester, UK, who advised P&G on the design of the study, but was not involved in carrying it out.

To develop the cosmetic – which consists of a regimen of three creams sold as Olay Pro-x – P&G used DNA microarrays to screen a range of existing cosmetic ingredients and identify those that changed the expression of a number of genes involved in skin ageing.

What the experts want

Before testing the resulting product, the firm consulted a panel of eight dermatologists, including Griffiths, and asked them what evidence they would need to be convinced that it worked.

The panel's first suggestion was that the product be tested over a prolonged period of time, around eight weeks. "Then we said, 'You're also going to have to go up against the clinical benchmark: tretinoin [trans-retinoic-acid],'" says panel member Stephen Mandy, a practising dermatologist based in Florida and a volunteer professor at the University of Miami. "There was this kind of hushed silence. Then they agreed to do it."

P&G isn't the first cosmetics firm to make public a scientific trial of a skincare product. In 2007, Boots in the UK made headlines when it compared its "Protect and Perfect" lotion with retinoic acid in a 12-day trial and showed that there was less sun damage in biopsies of skin treated with Protect and Perfect.

But P&G's latest result is the first long-term trial that has shown a cosmetic product to be as effective as retinoic acid. A longer-term trial of Protect and Perfect also produced a positive result, but only in comparison with a placebo moisturiser, not retinoic acid.

Wrinkle depth

In the current study, 99 women volunteers were given a regimen of three Olay Pro-x products, and 97 were prescribed tretinoin. The depth of their wrinkles was assessed before and after the treatments, and those assessing them were not told which product the women were using.

After eight weeks, the women using Pro-x showed a significant improvement in the appearance of their wrinkles compared with those using tretinoin. The women also tolerated Pro-x better than tretinoin, which caused irritation in some of the women.

Some of the volunteers were followed for a further 16 weeks, after which both treatments were judged to have improved the appearance of wrinkles to about the same extent.

"This is the first time that a cosmetic product has been tested head-to-head against a drug product over a long period of time and they've shown parity," says Mandy. "This is pretty landmark stuff."

Medicine or make-up?

It's not only researchers who advised P&G that are impressed. "I'm delighted somebody has done a real study and that they're setting about this with a scientific method," says Richard Weller , a dermatologist at the University of Edinburgh, UK. "I'm hoping that the public will fall for hard data and base their decisions on that."

But if Olay Pro-x works as well as a drug, should it be classified as one? P&G don't have to worry about that in the US: there, it is already on sale, and its components have previously been classified as cosmetic ingredients, meaning that it can be marketed as a cosmetic product.

A similar argument may well hold in the UK. "As long as you're not talking about diseases, the product remains a cosmetic, unless you have in it an ingredient that is only available on prescription," says Chris Flower, director of the UK's Cosmetic, Toiletry and Perfumery Association.

But Weller says the new finding could prevent Olay Pro-x from being launched as a cosmetic in Europe. He says that the European Cosmetics Directive considers a product that has a significant effect to be more than just a cosmetic. "Here they are saying something is as good as retinoic acid, which is a prescription drug," he says.

Reference: British Journal of Dermatology, DOI: 10.1111/j.1365-2133.2009.09436.x

Wanted: Volunteers, All Pregnant

By PAM BELLUCK

The woman sent by government scientists visited the Queens apartment repeatedly before finding anyone home. And the person who finally answered the door - a 30-year-old Colombian-born waitress named Alejandra - was wary.

Although Alejandra was exactly what the scientists were looking for - a pregnant woman - she was "a bit scared," she said, about giving herself and her unborn child to science for 21 years.

Researchers would collect and analyze her vaginal fluid, toenail clippings, breast milk and other things, and ask about everything from possible drug use to depression. At the birth, specimen collectors would scoop up her placenta and even her baby's first feces for scientific posterity.

"Nowadays there are so many scams," Alejandra said in Spanish, and her husband, José, "initially didn't want me to do the study." (Scientists said research confidentiality rules required that her last name be withheld.) But she ultimately decided that participating would "help the next generation."

Chalk one up for the scientists, who for months have been dispatching door-to-door emissaries across the country to recruit women like Alejandra for an unprecedented undertaking: the largest, most comprehensive long-term study of the health of children, beginning even before they are born.

Authorized by Congress in 2000, the National Children's Study began last January, its projected cost swelling to about $6.7 billion. With several hundred participants so far, it aims to enroll 100,000 pregnant women in 105 counties, then monitor their babies until they turn 21.

It will examine how environment, genes and other factors affect children's health, tackling questions subject to heated debate and misinformation. Does pesticide exposure, for example, cause asthma? Do particular diets or genetic mutations lead to autism?

"This is a very important study for understanding the health of our nation's children and for identifying factors that may play a role downstream in adult health," said Dr. Francis S. Collins, the director of the National Institutes of Health, which is overseeing the study.

But while the idea is praised by many experts, the study has also stirred controversy over its cost and content.

In August, the Senate committee overseeing financing for the study accused it of "a serious breach of trust" for not disclosing that the initial price tag of $3.1 billion would more than double, and said the study needed to release more information if it wanted to get "any" financing in the next budget year.

And an independent panel of experts and some members of the study's own advisory committee say it misses important opportunities to help people and communities - emphasizing narrower medical questions over concerns like racial and ethnic health differences, leaving unresolved crucial ethical questions concerning what to tell participants and communities about test results.

"This study is of the magnitude of the accelerator in CERN, or a trip to the moon - a really big science issue," said Milton Kotelchuck, a professor at the Boston University School of Public Health and a member of the independent panel. "But if you have a flawed beginning, then you've got 20 years of working on a flawed study."

Officials are making changes, putting all but the pilot phase, to involve 37 locations, on hold while conducting an inquiry into the cost and scientific underpinnings, Dr. Collins said. Some data may no longer be collected if "we can't afford" it, he said, and every aspect will receive "the closest possible scrutiny."

The study is far from its plan of recruiting 250 babies a year for four or five years in each community. By December, 510 women were enrolled and 83 babies were born in the first seven locations, including Orange County, Calif., and Salt Lake County, Utah.

That was after knocking on nearly 64,000 doors, screening 27,000 women and finding 1,000 who were pregnant and in their first trimester (and therefore eligible).

Dr. Collins said there were "unexpected difficulties in the number of houses that have to be visited to get enough babies" - 40 houses per enrolled woman, instead of the expected 14.

The time and information required from families could also make the study "too burdensome to be conducted the way it is," said Dr. Susan Shurin, former acting director of the National Institute of Child Health and Human Development, part of the National Institutes of Health and the study's supervising agency. The fear is women will "go 'Oh no, you again,' and slam the door in your face."

Specimens include blood, urine, hair and saliva from pregnant women, babies and fathers; dust from women's bedsheets; tap water; and particles on carpets and baseboards. They are sent to laboratories (placentas to Rochester, N.Y., for example), prepared for long-term storage, and analyzed for chemicals, metals, genes and infections.

Participants provide the names and phone numbers of relatives and friends, so researchers can find them if they move. As children grow, scientists, including outside experts, can cross-reference information about their medical conditions, behavioral development and school performance.

Clues could emerge if, for example, developmentally disabled children in both rural Alabama and suburban California show similar genetic patterns or chemical exposure.

"The task in selling this study is going to be to say we realize that this is audacious" and "seriously hard to do, but this is hugely important," said Dr. Ellen Wright Clayton, director of the Center for Biomedical Ethics and Society at Vanderbilt University and part of the independent panel and the study's advisory committee. "I'm hopeful some of the deficiencies can be addressed."

Selling the study presents different challenges everywhere.

In affluent, highly educated Waukesha County, Wis., the study is advertised on movie screens, yard signs and parade banners.

But in the hog-farm-and-Butterball-turkey-plant territory of Duplin County, N.C., where scientists have to enroll nearly a third of the 800 babies born each year, some women are "concerned about questions they may be answering and how they may sound answering those questions," said Dr. Roland Draughn, a local obstetrician.

Nancy Dole, a co-principal investigator in Duplin, said "we had to reassure" residents that "the purpose is not to make the county look bad."

Organizers have visited child car-seat installation events, church groups, even Latino men's soccer teams. Some women have volunteered, even ones who are not pregnant, bringing their children to the study's Duplin headquarters, a former video store.

But others would hesitate if approached.

"Twenty-one years, that's a long time," said Wanda Johnson, 37, a nursing-home aide with four children. "I may say yes, and then tomorrow, I don't want to be bothered."

In Queens, with over 2 million people and 30,000 births a year, recruiting 250 might seem easy. And some pregnant women, like Amy Saez, 28, said that if asked to participate, "I would totally be down with that because I'd become a part of science and history." But recruiters confront a jumble of languages and cultures, calling telephone translation lines to communicate in Urdu, Nepalese and Russian, for example.

And they have to "knock on each and every door in a building until they learn who lives there," said Dr. Philip Landrigan, chairman of preventive medicine at Mount Sinai medical school and the principal investigator in Queens. They buzz random apartments to get into buildings, "buttonhole people coming out, talk to doormen, supers," he said. For recruiters' safety, door-knocking stops at 8 p.m.

Soon, said Dr. Steven Hirschfeld, appointed the study's director when the original leader left under criticism, new recruiting methods will be tried, including having doctors encourage patients to enroll. That was previously rejected because investigators felt doctor-referred patients would exclude some women, like those not getting prenatal care.

Besides looking at widespread conditions, like diabetes, the study will consider regional differences. Maureen Durkin, principal investigator in Waukesha County, Wis., wonders if radium in the county's water, and houses built on "farm fields that may be contaminated with nitrates and atrazine," have different health consequences than pollution or industrial chemicals in Queens.

Health authorities in Duplin County, N.C., are concerned about "so many hog lagoons and poop everywhere," said Shannon Brewer, a health department nurse, who also worries that many women there fail to breastfeed because "at the turkey factory, they just can't step out of line to pump."

In Flushing, Queens, Alejandra, who gave birth to Isabella in August, is breastfeeding. But she said she was "afraid of the baby getting too many vaccines." She quit smoking after getting pregnant, but her husband, 34, a golf instructor, smokes in their bathroom.

Joseph Gilbert, a study employee who has been interviewing and collecting samples from Alejandra, said study protocol limited his ability to urge participants to change health habits.

But study officials are trying to determine what information to give participants and when. Some experts say people should get results of their chemical or genetic tests only if medical treatments exist because otherwise it only causes anxiety. Others agree with Patricia O'Campo, a member of the study's advisory committee and the independent panel, who says the study should be "less ivory towerish" and disclose more information to families and communities.

In this and other aspects of the study, "changes have to be made, and maybe some very big changes," Dr. O'Campo said. "I think it could be so much more." *Dabrali Jimenez contributed reporting.*

Scientists discover molecular pathway for organ tissue regeneration and repair

CINCINNATI -- Scientists have discovered a molecular pathway that works through the immune system to regenerate damaged kidney tissues and may lead to new therapies for repairing injury in a number of organs systems. The findings, reported in this week's Proceedings of the National Academy of Sciences (PNAS), come from collaborative research led by Cincinnati Children's Hospital Medical Center and the Brigham & Women's Hospital of Harvard Medical School.

The study may have significant medical ramifications as currently there are no effective treatments for acute kidney injury – a growing problem in hospitals and clinics, according to the study's senior co-authors, Richard Lang, Ph.D., a researcher in the divisions of Pediatric Ophthalmology and Developmental Biology at Cincinnati Children's, and Jeremy Duffield, M.D., Ph.D., a researcher at Brigham and Women's Hospital. Acute kidney injury is a significant cause of kidney disease, cardiovascular complications and early death, affecting as many as 16 million children and adults in the United States.

The new molecular repair pathway involves white blood cells called macrophages – part of the immune system – that respond to tissue injury by producing a protein called Wnt7b. Scientists identified the macrophage-Wnt7b pathway during experiments in mice with induced kidney injury. Wnt7b is already known to be important to the formation of kidney tissues during embryonic organ development. In this study the scientists found the protein helped initiate tissue repair and regeneration in injured kidneys.

"Our findings suggest that by migrating to the injured kidney and producing Wnt7b, macrophages are re-establishing an early molecular program for organ development that also is beneficial to tissue repair," said Dr. Lang. "This study also indicates the pathway may be important to tissue regeneration and repair in other organs."

Wnt7b is part of the Wnt family of proteins, which are known to help regulate cells as they proliferate, grow and become specific cell types for the body. Wnt proteins have also been linked to the regulation of stem cells in bone marrow and skin, which suggested to researchers of the current study that Wnt might have a role in tissue regeneration. The researchers conducted a number of experiments of kidney injury in mice to identify the repair pathway, finding that:

* Silencing macrophage white blood cells through a process called ablation reduced the response level of Wnt proteins to injured kidney cells.

* Deleting the Wnt7b protein from macrophages diminished normal tissue repair functions in injured kidneys.

* Injecting into the injured kidneys a protein calked Dkk2, which interacts with and is known to help regulate the Wnt pathway during embryonic development, enhanced the macrophage-Wnt7b repair process. It also restored epithelial surface cells that line internal kidney surfaces and suggested a therapeutic potential for the pathway.

Drs. Lang and Duffield said the repair pathway may benefit other injured organs because macrophages act somewhat like a universal emergency responder in the body, rushing to injured tissues wherever damage occurs. Another factor is the central role the Wnt pathway plays in cell regulation and function throughout the body.

Other collaborating institutions in the study include: the Department of Structural Biology , St, Jude Children's Hospital, Memphis, Tenn.; the departments of Internal Medicine and Molecular Biology, University of Texas Southwest Medical Center; Department of Molecular and Developmental Biology, Albert Einstein College of Medicine of Yeshiva University, Bronx, N.Y.; Department of Molecular and Cellular Biology, Harvard University; the Visual Systems Group in the division of Pediatric Ophthalmology at Cincinnati Children's; and the Department of Ophthalmology, University of Cincinnati.

Funding support came from the National Institutes of Health, the American Society of Nephrology Gottschalk Award, the Genzyme Renal Initiatives Program, a National Taiwan Merit Award, and the Abrahamson Pediatric Eye Institute Endowment at Cincinnati Children's.

'Perfect' liquid hot enough to be quark soup

Protons, neutrons melt to produce 'quark-gluon plasma' at RHIC

UPTON, NY - Recent analyses from the [http://www.bnl.gov/rhic/] Relativistic Heavy Ion Collider (RHIC), a 2.4-mile-circumference "atom smasher" at the U.S. Department of Energy's (DOE) Brookhaven National Laboratory, establish that collisions of gold ions traveling at nearly the speed of light have created matter at a temperature of about 4 trillion degrees Celsius - the hottest temperature ever reached in a laboratory, about 250,000 times hotter than the center of the Sun. This temperature, based upon measurements by the PHENIX collaboration at RHIC, is higher than the temperature needed to melt protons and neutrons into a plasma of quarks and gluons. Details of the findings will be published in Physical Review Letters.

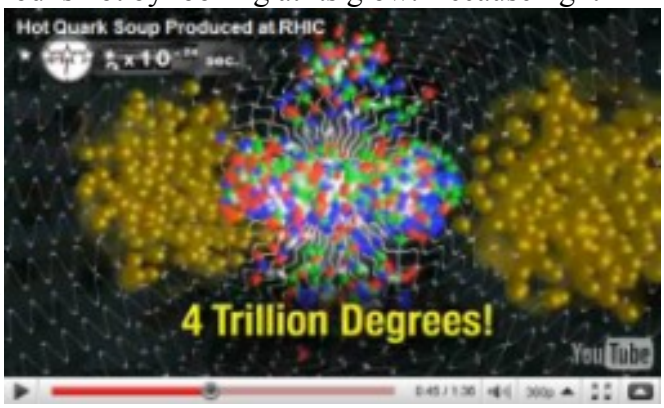
These new temperature measurements, combined with other observations analyzed over nine years of operations by RHIC's four experimental collaborations - BRAHMS, PHENIX, PHOBOS, and STAR - indicate

that RHIC's gold-gold collisions produce a freely flowing liquid composed of quarks and gluons. Such a substance, often referred to as quark-gluon plasma, or QGP, filled the universe a few microseconds after it came into existence 13.7 billion years ago. At RHIC, this liquid appears, and the quoted temperature is reached, in less time than it takes light to travel across a single proton.

"This research offers significant insight into the fundamental structure of matter and the early universe, highlighting the merits of long-term investment in large-scale, basic research programs at our national laboratories," said Dr. William F. Brinkman, Director of the DOE Office of Science. "I commend the careful approach RHIC scientists have used to gather detailed evidence for their claim of creating a truly remarkable new form of matter."

According to Steven Vigdor, Brookhaven's Associate Laboratory Director for Nuclear and Particle Physics, who oversees the RHIC research program, "These data provide the first measurement of the temperature of the quark-gluon plasma at RHIC."

Scientists measure the temperature of hot matter by looking at the color, or energy distribution, of light emitted from it - similar to the way one can tell that an iron rod is hot by looking at its glow. Because light interacts very little with the hot liquid produced at RHIC, it bears accurate witness to the early cauldron-like conditions created within.



Said Vigdor, "The temperature inferred from these new measurements at RHIC is considerably higher than the long-established maximum possible temperature attainable without the liberation of quarks and gluons from their normal confinement inside individual protons and neutrons. "However," he added, "the quarks and gluons in the matter we see at RHIC behave much more cooperatively than the independent particles initially predicted for QGP."

Freeing Quarks and Gluons Physicists melted protons and neutrons in the Relativistic Heavy Ion Collider at the Brookhaven National Laboratory in an effort to create quark-gluon plasma.

Hot gas vs. hot liquid

Scientists believe that a plasma of quarks and gluons existed a few microseconds after the birth of the universe, before cooling and condensing to form the protons and neutrons that make up all the matter around us - from individual atoms to stars, planets, and people. Although the matter produced at RHIC survives for much less than a billionth of a trillionth of a second, its properties can be determined using RHIC's highly sophisticated detectors to look at the thousands of particles emitted during its brief lifetime. The measurements provide new insights into Nature's strongest force - in essence, what holds all the protons and neutrons of the universe together.

Predictions made prior to RHIC's initial operations in 2000 expected that the quark-gluon plasma would exist as a gas. But surprising and definitive data from RHIC's first three years of operation, presented by RHIC scientists in April 2005, showed that the matter produced at RHIC behaves as a liquid, whose constituent particles interact very strongly among themselves. This liquid matter has been described as nearly "perfect" in the sense that it flows with almost no frictional resistance, or viscosity. Such a "perfect" liquid doesn't fit with the picture of "free" quarks and gluons physicists had previously used to describe QGP.

In the papers published in 2005, RHIC physicists laid out a plan of crucial measurements to clarify the nature and constituents of the "perfect" liquid. Measuring the temperature early in the collisions was one of those goals. Models of the evolution of the matter produced in RHIC collisions had suggested that the initial temperature might be high enough to melt protons, but a more direct measurement of the temperature required detecting photons - particles of light - emitted near the beginning of the collision, which travel outward undisturbed by their surroundings.

"This was an extraordinarily challenging measurement," explained Barbara Jacak, a professor of physics at Stony Brook University and spokesperson for the PHENIX collaboration. "There are many ways that photons can be produced in these violent collisions. We were able to 'eliminate' the contribution from these other sources by exploiting RHIC's flexibility to measure them directly and to make the same measurement in collisions of protons, rather than of gold nuclei. Thus we could pin down excess production in the gold-gold collisions, and determine the temperature of the matter that radiated the excess photons. By matching theoretical models of the expanding plasma to the data, we can determine that the initial temperature of the 'perfect' liquid has reached about four trillion degrees Celsius."

Moving forward

The discoveries at RHIC have led to compelling new questions in the field of quantum chromodynamics (QCD), the theory that describes the interactions of the smallest known components of the atomic nucleus. To probe these and other questions and conduct detailed studies of the plasma, Brookhaven physicists are planning to [http://www.bnl.gov/bnlweb/pubaf/pr/PR_display.asp?prID=741] upgrade RHIC over the next few years to increase its collision rate and detector capabilities.

"These technical improvements will facilitate studies of rare signals providing measurements of even better precision on temperature, viscosity, and other basic properties of the nearly perfect liquid quark-gluon plasma created at RHIC," Vigdor said.

Research at RHIC is funded primarily by the U.S. Department of Energy's Office of Science and by various national and international collaborating institutions. For a complete list of RHIC funders, go to: [http://www.bnl.gov/rhic/funding.asp] http://www.bnl.gov/rhic/funding.asp.

Q & A

Bras and Cancer

By C. CLAIBORNE RAY

Victoria Roberts

Q. Is there any truth to the Internet rumor that the incidence of breast cancer is more than 100 times greater in women who always wear bras than in women who never wear bras?

A. "The short answer is no," Dr. Ted Gansler, director of medical content for the American Cancer Society, replied in an e-mail message.

There is no scientifically credible evidence of this, he said, and the proposed mechanism - that bras prevent elimination of toxins by blocking lymph flow - is not in line with scientific concepts of how breast cancer develops.

Internet traffic on the issue is mostly inspired by one study with several scientific flaws, Dr. Gansler said. The study, never published in a peer-reviewed journal, did not adjust for known breast cancer risk factors that might be associated with bra-wearing behavior, like weight and age. Also, study participants knew the hypothesis before taking the survey.

"Because the idea of bras' causing breast cancer is so scientifically implausible, it seems unlikely that researchers will ever spend their time and resources to test it in a real epidemiological study," Dr. Gansler said.

He and colleagues compared National Cancer Institute data on breast cancer risk for women treated for melanoma who had several underarm lymph nodes removed and those who did not. The surgery, which is known to block lymph drainage from breast tissue, did not detectably increase breast cancer rates, the study found, meaning that it is extremely unlikely that wearing a bra, which affects lymph flow minimally if at all, would do so.

On Crete, New Evidence of Very Ancient Mariners

By JOHN NOBLE WILFORD

Early humans, possibly even prehuman ancestors, appear to have been going to sea much longer than anyone had ever suspected.

That is the startling implication of discoveries made the last two summers on the Greek island of Crete. Stone tools found there, archaeologists say, are at least 130,000 years old, which is considered strong evidence for the earliest known seafaring in the Mediterranean and cause for rethinking the maritime capabilities of prehuman cultures.

Crete has been an island for more than five million years, meaning that the toolmakers must have arrived by boat. So this seems to push the history of Mediterranean voyaging back more than 100,000 years, specialists in Stone Age archaeology say. Previous artifact discoveries had shown people reaching Cyprus, a few other Greek islands and possibly Sardinia no earlier than 10,000 to 12,000 years ago.

The oldest established early marine travel anywhere was the sea-crossing migration of anatomically modern Homo sapiens to Australia, beginning about 60,000 years ago. There is also a suggestive trickle of evidence, notably the skeletons and artifacts on the Indonesian island of Flores, of more ancient hominids making their way by water to new habitats.

Even more intriguing, the archaeologists who found the tools on Crete noted that the style of the hand axes suggested that they could be up to 700,000 years old. That may be a stretch, they conceded, but the tools

resemble artifacts from the stone technology known as Acheulean, which originated with prehuman populations in Africa.

More than 2,000 stone artifacts, including the hand axes, were collected on the southwestern shore of Crete, near the town of Plakias, by a team led by Thomas F. Strasser and Eleni Panagopoulou. She is with the Greek Ministry of Culture and he is an associate professor of art history at Providence College in Rhode Island. They were assisted by Greek and American geologists and archaeologists, including Curtis Runnels of Boston University.

HARDWARE Stone tools found on Crete are evidence of early sea voyages. **Nicholas Thompson and Chad DiGregorio**

Dr. Strasser described the discovery last month at a meeting of the Archaeological Institute of America. A formal report has been accepted for publication in Hesparia, the journal of the American School of Classical Studies in Athens, a supporter of the fieldwork.

The Plakias survey team went in looking for material remains of more recent artisans, nothing older than 11,000 years. Such artifacts would have been blades, spear points and arrowheads typical of Mesolithic and Neolithic periods. “We found those, then we found the hand axes,” Dr. Strasser said last week in an interview, and that sent the team into deeper time. “We were flummoxed,” Dr. Runnels said in an interview. “These things were just not supposed to be there.”

Word of the find is circulating among the ranks of Stone Age scholars. The few who have seen the data and some pictures - most of the tools reside in Athens - said they were excited and cautiously impressed. The research, if confirmed by further study, scrambles timetables of technological development and textbook accounts of human and prehuman mobility.

Ofer Bar-Yosef, an authority on Stone Age archaeology at Harvard, said the significance of the find would depend on the dating of the site. “Once the investigators provide the dates,” he said in an e-mail message, “we will have a better understanding of the importance of the discovery.”

Dr. Bar-Yosef said he had seen only a few photographs of the Cretan tools. The forms can only indicate a possible age, he said, but “handling the artifacts may provide a different impression.” And dating, he said, would tell the tale.

Dr. Runnels, who has 30 years’ experience in Stone Age research, said that an analysis by him and three geologists “left not much doubt of the age of the site, and the tools must be even older.”

The cliffs and caves above the shore, the researchers said, have been uplifted by tectonic forces where the African plate goes under and pushes up the European plate. The exposed uplifted layers represent the sequence of geologic periods that have been well studied and dated, in some cases correlated to established dates of glacial and interglacial periods of the most recent ice age. In addition, the team analyzed the layer bearing the tools and determined that the soil had been on the surface 130,000 to 190,000 years ago.

Dr. Runnels said he considered this a minimum age for the tools themselves. They include not only quartz hand axes, but also cleavers and scrapers, all of which are in the Acheulean style. The tools could have been made millenniums before they became, as it were, frozen in time in the Cretan cliffs, the archaeologists said.

Dr. Runnels suggested that the tools could be at least twice as old as the geologic layers. Dr. Strasser said they could be as much as 700,000 years old. Further explorations are planned this summer.

The 130,000-year date would put the discovery in a time when Homo sapiens had already evolved in Africa, sometime after 200,000 years ago. Their presence in Europe did not become apparent until about 50,000 years ago.

Archaeologists can only speculate about who the toolmakers were. One hundred and thirty thousand years ago, modern humans shared the world with other hominids, like Neanderthals and Homo heidelbergensis. The Acheulean culture is thought to have started with Homo erectus.

The standard hypothesis had been that Acheulean toolmakers reached Europe and Asia via the Middle East, passing mainly through what is now Turkey into the Balkans. The new finds suggest that their dispersals were not confined to land routes. They may lend credibility to proposals of migrations from Africa across the Strait of Gibraltar to Spain. Crete’s southern shore where the tools were found is 200 miles from North Africa.

“We can’t say the toolmakers came 200 miles from Libya,” Dr. Strasser said. “If you’re on a raft, that’s a long voyage, but they might have come from the European mainland by way of shorter crossings through Greek islands.”

But archaeologists and experts on early nautical history said the discovery appeared to show that these surprisingly ancient mariners had craft sturdier and more reliable than rafts. They also must have had the cognitive ability to conceive and carry out repeated water crossing over great distances in order to establish sustainable populations producing an abundance of stone artifacts.

Autism's earliest symptoms not evident in children under 6 months

Condition is characterized by a slow decline rather than an abrupt loss of skills, study says

SACRAMENTO, Calif. - A study of the development of autism in infants, comparing the behavior of the siblings of children diagnosed with autism to that of babies developing normally, has found that the nascent symptoms of the condition — a lack of shared eye contact, smiling and communicative babbling — are not present at 6 months, but emerge gradually and only become apparent during the latter part of the first year of life.

Researchers conducted the study over five years by painstakingly counting each instance of smiling, babbling and eye contact during examinations until the children were 3. They found that by 12 months the two groups' development had diverged significantly. Intentional social and communicative behavior among children developing normally increased while among infants later diagnosed with autism it decreased dramatically. The study is published online early and will appear in the March issue of the Journal of the American Academy of Child & Adolescent Psychiatry.

"This study provides an answer to when the first behavioral signs of autism become evident," said Sally Ozonoff, the study's lead author, a professor of psychiatry and behavioral sciences and a researcher with the UC Davis MIND Institute. "Contrary to what we used to think, the behavioral signs of autism appear later in the first year of life for most children with autism. Most babies are born looking relatively normal in terms of their social abilities but then, through a process of gradual decline in social responsiveness, the symptoms of autism begin to emerge between 6 and 12 months of age."

Autism is a pervasive developmental disorder of deficits in social skills and communication, as well as in repetitive and restricted behaviors, with onset occurring prior to age 3. Abnormal brain development, probably beginning prenatally, is known to be fundamental to the behaviors that characterize autism. Current estimates place the condition's incidence at between 1 in 100 and 1 in 110 children in the United States.

Children with a sibling already diagnosed with autism are known to be among those at greatest risk of developing the disorder. The current study included 25 high-risk children who met criteria for autism at 3 years of age, matched with 25 low risk peers who were developing normally. It was conducted at the MIND Institute and the University of California, Los Angeles. The sole inclusion criterion for the high-risk group was having a sibling with autism; low-risk participants had to have been born after 36 weeks gestation and have no autistic family members.

The children's development was evaluated at 6, 12, 18, 24 and 36 months of age using a series of widely implemented diagnostic tools, including the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview-Revised (ADI-R). Examiners were not told which babies were at high- or low-risk when evaluating the participants' development.

The researchers found that there were few discernable differences between the two groups at the outset but that after six months, 86 percent of the infants who developed autism showed declines in social communication that were outside the range for typical development. "After six months," the study found, "the autism spectrum disorder group showed a rapid decline in eye contact, social smiling, and examiner-rated social responsiveness." Group differences were significant by 12 months in eye contact and social smiling and all other measures by 18 months, the study found.

The study is notable because of the accuracy and precision of its prospective methodology, assiduously recording exact numbers of social and communicative behaviors during lab visits. Previously, researchers have constructed evidence of autism's earliest manifestations by interviewing parents about when they believed their children's symptoms first arose or by reviewing home movies for clues to when children begin exhibiting symptoms of autism.

"Until now, research has relied on asking parents when their child reached developmental milestones. But that can be really difficult to recall, and there is a phenomenon called the "telescoping effect" where people usually say that they remember something happening more recently than when it occurred," Ozonoff said. In addition parents frequently will turn off the video camera when their children are behaving poorly — precisely when autistic symptoms may appear.

Ozonoff said that the study provides a deeper understanding for parents, caregivers and health-care providers and for future research of the developmental trajectory for very young children with autism.

"We need to be careful about how we screen, and we need to know what we're looking for," Ozonoff said. "This study tells us that screening for autism early in the first year of life probably is not going to be successful because there isn't going to be anything to notice. It also tells us that we should be focusing on social behaviors in our screening, since that is what declines early in life."

"This study also found that the loss of skills continues into the second and third year of life," she said. "So it may not be adequate, as the American Academy of Pediatrics currently suggests, that providers screen for autism twice before the end of the second year. Autism has a slow, gradual onset of symptoms, rather than a very abrupt loss of skills."

"Screening may need to continue into the third year of life, since symptom emergence takes place over a long time. If a child starts exhibiting a declining trajectory and a sustained reduction in social communication we want to refer them into therapy, especially if they are at risk," Ozonoff said, "even before we might be able to make a definitive diagnosis."

Ozonoff said that the study does not address the etiology of autism or causality. In this study, the infants who participated were at high risk due to having strong family histories of autism, suggesting that genetics play a major role in the later autism diagnoses, despite the fact that their symptoms were not apparent at birth.

Other study authors include Ana-Maria Iosif, Fam Baguio, Ian C. Cook, Monique Moore Hill, Mary Beth Steinfeld, Sally J. Rogers, Sarabjit Sangha and Gregory S. Young of UC Davis and Ted Hutman, Agata Rozga and Marian Sigman of the University of California, Los Angeles.

The study was funded by grants from the National Institute of Mental Health of the National Institutes of Health.

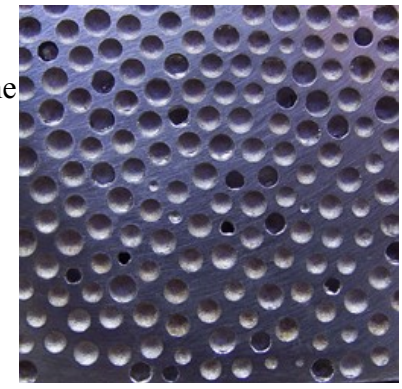
New Material Mimics Bone To Create Better Biomedical Implants

Matt Shipman | News Services | 919.515.6386

A "metal foam" that has a similar elasticity to bone could mean a new generation of biomedical implants that would avoid bone rejection that often results from more rigid implant materials, such as titanium. Researchers at North Carolina State University have developed the metal foam, which is even lighter than solid aluminum and can be made of 100 percent steel or a combination of steel and aluminum.

In a new paper, researchers have reported recent findings that, in addition to the extraordinary high-energy absorption capability and light weight of their novel composite foams, the "modulus of elasticity" of the foam is very similar to that of bone. Modulus of elasticity measures a material's ability to deform when pressure is applied and then return to its original shape when pressure is removed. The rough surface of the foam would also foster bone growth into the implant, improving the strength of implant.

Modulus of elasticity, which is measured in gigapascals (GPa), is extremely important for biomedical implants, explains Dr. Afsaneh Rabiei, an associate professor of mechanical and aerospace engineering and an associate faculty member of biomedical engineering at NC State and co-author of the paper.



Composite foam made out of 100 percent steel using powder metallurgy technique.

"When an orthopedic or dental implant is placed in the body to replace a bone or a part of a bone, it needs to handle the loads in the same way as its surrounding bone," Rabiei says. "If the modulus of elasticity of the implant is too much bigger than the bone, the implant will take over the load bearing and the surrounding bone will start to die. This will cause the loosening of the implant and eventually ends in failure. This is known as "'stress shielding.'" When this happens, the patient will need a revision surgery to replace the implant. Our composite foam can be a perfect match as an implant to prevent stress shielding," Rabiei explains.

To give an idea of the difference between the modulus of elasticity of bone and that of traditional implants, bone has a modulus of between 10 and 30 GPa – while titanium has a modulus of approximately 100 GPa. The new composite foam has a modulus that is consistent with bone, and is also relatively light because it is porous.

The rough surface of the metal foam, Rabiei says, "will bond well with the new bone formed around it and let the body build inside its surface porosities. This will increase the mechanical stability and strength of the implant inside the body."

The research, "Evaluation of modulus of elasticity of composite metal foams by experimental and numerical techniques," was funded by the National Science Foundation and will be published in the March issue of Materials Science and Engineering A. The research was co-authored by Rabiei and former NC State Ph.D. student L. Vendra. ***-shipman-***

Note to editors: *"Evaluation of modulus of elasticity of composite metal foams by experimental and numerical techniques" L. Vendra, Afsaneh Rabiei, North Carolina State University March 2010, Materials Science and Engineering A*

Cancer publishes study confirming disparity in breast cancer treatment

Study confirms previous results of government health plans in commercial plan population

WILMINGTON, Del - Cancer, the peer-reviewed international journal of the American Cancer Society, has published a study conducted by HealthCore, Inc. in its Jan. 1 edition, demonstrating disparities in breast cancer treatment between commercially insured African-American and white women. The HealthCore study reiterates the findings of previous studies - conducted in populations using government health programs - that African-American women are diagnosed in later stages of the disease. Breast cancer is the second most common cause of cancer death in white and African-American women in the United States.

"This study demonstrates that disparities in breast cancer care exist even when patients have access to employer-provided healthcare," said Dr. Joe Singer, HealthCore vice president for clinical affairs. "A key takeaway from our study is that African-American women were diagnosed with breast cancer at younger ages, but in later stages of breast cancer, when chances of survival diminish greatly."

The study, funded by Amgen, was conducted in collaboration with Blue Cross and Blue Shield of Georgia and the American Cancer Society. HealthCore is working with Blue Cross and Blue Shield of Georgia and the American Cancer Society to further evaluate the study to understand more about the women who are newly diagnosed with breast cancer so the health plan can determine better ways to communicate with them and their physicians in an attempt to diminish the disparities.

The HealthCore study also found that not all women who tested positive for hormone receptor cancer received anti-estrogen therapy, which is a standard of care set by guidelines established by the National Comprehensive Cancer Network and the American Cancer Society. Of those women who did test positive, white women were more likely than African-American women to receive anti-estrogen therapy.

Specifically, the study found:

* White women (55.2 percent) were more likely than African- American women (38.4 percent) to be diagnosed with stage 0 or stage I disease.

* Twice as many African-American women (6.1 percent) compared with white women (3.6 percent) were diagnosed with stage IV disease.

* Among women who tested positive for hormone receptor cancer, African-American women were less likely to receive treatment, such as aromatase inhibitors or tamoxifen.

* White women were twice as likely to receive anti-estrogen therapy compared with African-American women, after adjusting for age, cancer stage, and social economic status.

"While treatment for depression and anxiety occurred in both groups, less than half of those women had notes in their medical charts to follow-up with their primary care physician and only one women was referred to a mental health professional," said Dr. Otis Brawley, chief medical officer for the American Cancer Society and study co-author. "Clearly, this is a health intervention needed for both African-American and white women."

About the study

The study pool of 3,017 women was identified from a medical claims database with information extracted from medical chart data on 766 women. Of those patients who had race data, 79.8 percent were white and 16.6 percent were African-American. Health plan claims data were then linked to information abstracted from medical charts to measure age, use of medications and to obtain detailed clinical information regarding their breast cancer and co-morbid medical conditions present at the time of the breast cancer diagnosis. HealthCore also collected data on the cancer-specific treatment received, adverse events, supportive care and oncologist follow-up communication with primary care physicians.

Lack of morning light keeping teenagers up at night

First field study shows lack of exposure to morning light delays sleep in teens

Troy, N.Y - The first field study on the impact of light on teenagers' sleeping habits finds that insufficient daily morning light exposure contributes to teenagers not getting enough sleep.

"As teenagers spend more time indoors, they miss out on essential morning light needed to stimulate the body's 24-hour biological system, which regulates the sleep/wake cycle," reports Mariana Figueiro, Ph.D., Assistant Professor and Program Director at Rensselaer Polytechnic Institute's Lighting Research Center (LRC) and lead researcher on the new study.

"These morning-light-deprived teenagers are going to bed later, getting less sleep and possibly under-performing on standardized tests. We are starting to call this the teenage night owl syndrome."

In the study just published in Neuroendocrinology Letters, Dr. Figueiro and LRC Director Dr. Mark Rea found that eleven 8th grade students who wore special glasses to prevent short-wavelength (blue) morning light from reaching their eyes experienced a 30-minute delay in sleep onset by the end of the 5-day study.

"If you remove blue light in the morning, it delays the onset of melatonin, the hormone that indicates to the body when it's nighttime," explains Dr. Figueiro. "Our study shows melatonin onset was delayed by about 6

minutes each day the teens were restricted from blue light. Sleep onset typically occurs about 2 hours after melatonin onset."

Disrupting Biological Rhythms

The problem is that today's middle and high schools have rigid schedules requiring teenagers to be in school very early in the morning. These students are likely to miss the morning light because they are often traveling to and arriving at school before the sun is up or as it's just rising. "This disrupts the connection between daily biological rhythms, called circadian rhythms, and the earth's natural 24-hour light/dark cycle," explains Dr. Figueiro.

In addition, the schools are not likely providing adequate electric light or daylight to stimulate this biological or circadian system, which regulates body temperature, alertness, appetite, hormones and sleep patterns. Our biological system responds to light much differently than our visual system. It is much more sensitive to blue light. Therefore, having enough light in the classroom to read and study does not guarantee that there is sufficient light to stimulate our biological system.

"According to our study, however, the situation in schools can be changed rapidly by the conscious delivery of daylight, which is saturated with short-wavelength, or blue, light," reports Dr. Figueiro.

First Field Study

Dr. Figueiro's research, sponsored by the U.S. Green Building Council and in part by a grant from a Trans-National Institutes of Health Genes, Environment and Health Initiative is the first field study to measure the impact of reduced morning blue light exposure on evening melatonin onset of teenagers attending school.

According to Dr. Figueiro, the results of this field study are significant because they validate controlled laboratory findings with actual field measurements of light that impact our biological system.

The field experiment was conducted at Smith Middle School in Chapel Hill, North Carolina, a school with good daylight design. The school building has south-facing skylights to deliver daylight to nearly all interior spaces throughout the day.

The study detailed in Neuroendocrinology Letters is part of a larger study where data on students was collected at both Smith Middle School in Chapel Hill, North Carolina, as well as Algonquin Middle School in Averill Park, New York.

The larger study is examining not only the impact of removing morning blue light, but also the seasonal impact and the increased evening light exposure during the spring months on teens' melatonin onset and sleep times.

Implications for School Design

Throughout her research, Dr. Figueiro has repeatedly come face-to-face with the enormous concern of parents over teenagers going to bed too late. "Our findings pose two questions: "How will we promote exposure to morning light and how will we design schools differently?" says Dr. Figueiro.

The study findings should have significant implications for school design. "Delivering daylight in schools may be a simple, non-pharmacological treatment for students to help them increase sleep duration," concludes Dr. Figueiro.

Light Therapy Can Reduce Health Risks of Shift Workers and Alzheimer's Patients

The new research has applications for more than 3 million shift workers and Alzheimer's patients who suffer from lack of a regular sleep pattern. Studies have shown that this lack of synchronization between a shift worker's rest and activity and light/dark patterns leads to a much higher risk of cardiovascular disease, diabetes, seasonal depression and cancer over decades.

As evidenced in prior studies by Dr. Figueiro, light therapy can also be used to improve sleep in Alzheimer's patients, who usually display uneven sleep patterns. "By removing light at certain times of day, and giving light at other times, you can synchronize the sleep/wake patterns of Alzheimer's patients with the light/dark pattern, providing them with more consolidated sleep," says Dr. Figueiro.

Team finds subtropical waters flushing through Greenland fjord

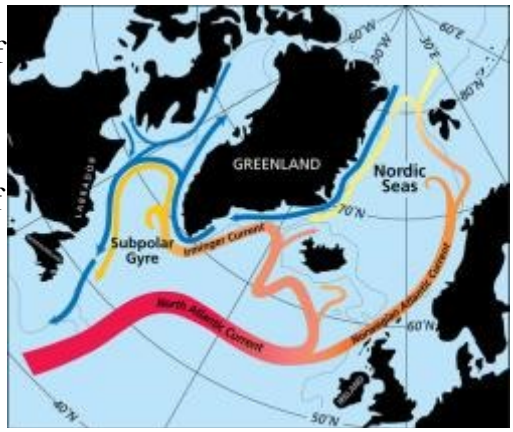
Waters from warmer latitudes — or subtropical waters — are reaching Greenland's glaciers, driving melting and likely triggering an acceleration of ice loss, reports a team of researchers led by Fiamma Straneo, a physical oceanographer from the Woods Hole Oceanographic Institution (WHOI).

"This is the first time we've seen waters this warm in any of the fjords in Greenland," says Straneo. "The subtropical waters are flowing through the fjord very quickly, so they can transport heat and drive melting at the end of the glacier."

Greenland's ice sheet, which is two-miles thick and covers an area about the size of Mexico, has lost mass at an accelerated rate over the last decade. The ice sheet's contribution to sea level rise during that time frame doubled due to increased melting and, to a greater extent, the widespread acceleration of outlet glaciers around

Greenland. While melting due to warming air temperatures is a known event, scientists are just beginning to learn more about the ocean's impact - in particular, the influence of currents - on the ice sheet.

"Among the mechanisms that we suspected might be triggering this acceleration are recent changes in ocean circulation in the North Atlantic, which are delivering larger amounts of subtropical waters to the high latitudes," says Straneo. But a lack of observations and measurements from Greenland's glaciers prior to the acceleration made it difficult to confirm.



The research team, which included colleagues from University of Maine, conducted two extensive surveys during July and September of 2008, collecting both ship-based and moored oceanographic data from Sermilik Fjord - a large glacial fjord in East Greenland.

Sermilik Fjord, which is 100 kilometers (approximately 62 miles) long, connects Helheim Glacier with the Irminger Sea. In 2003 alone, Helheim Glacier retreated several kilometers and almost doubled its flow speed.

Recent changes in ocean circulation in the North Atlantic are delivering larger amounts of subtropical waters to the high latitudes. A research team led by Fiamma Straneo, a physical oceanographer at Woods Hole Oceanographic Institution, found that subtropical waters are reaching Greenland's glaciers, driving melting and likely triggering an acceleration of ice loss. Melting ice also means more fresh water in the ocean, which could flood into the North Atlantic and disrupt a global system of currents, known as the Ocean Conveyor. **Jack Cook, Woods Hole Oceanographic Institution**

Deep inside the Sermilik Fjord, researchers found subtropical water as warm as 39 degrees Fahrenheit (4 degrees Celsius). The team also reconstructed seasonal temperatures on the shelf using data collected by 19 hooded seals tagged with satellite-linked temperature depth-recorders. The data revealed that the shelf waters warm from July to December, and that subtropical waters are present on the shelf year round.

"This is the first extensive survey of one of these fjords that shows us how these warm waters circulate and how vigorous the circulation is," says Straneo. "Changes in the large-scale ocean circulation of the North Atlantic are propagating to the glaciers very quickly — not in a matter of years, but a matter of months. It's a very rapid communication."

Straneo adds that the study highlights how little is known about ocean-glacier interactions, which is a connection not currently included in climate models.

"We need more continuous observations to fully understand how they work, and to be able to better predict sea-level rise in the future," says Straneo.

The paper was chosen for advanced online publication Feb. 14, 2010, by Nature Geosciences; it will also appear in the March 2010 printed edition of the journal. Co-authors of the work include WHOI postdoc David Sutherland (now of University of Washington), Gordon Hamilton and Leigh Stearns of the Climate Change Institute, University of Maine, Fraser Davidson and Garry Stenson of the Department of Fisheries and Oceans, St. John's, Newfoundland, Mike Hammill of the Department of Fisheries and Oceans, Mont-Joli, Quebec, and Aqqalu Rosing-Asvid of the Department of Birds and Mammals, Greenland Institute of Natural Resources. Canadian and Greenlandic colleagues contributed valuable data on the shelf, from tagged seals.

Funding for this research was provided by the National Science Foundation, WHOI's Ocean and Climate Change Institute Arctic Research Initiative, and NASA's Cryosperic Sciences Program.

The carbon cycle before humans

Two studies provide clearer picture of how carbon cycle was dramatically affected long ago

Geoengineering -- deliberate manipulation of the Earth's climate to slow or reverse global warming -- has gained a foothold in the climate change discussion. But before effective action can be taken, the Earth's natural biogeochemical cycles must be better understood.

Two Northwestern University studies, both published online recently by Nature Geoscience, contribute new -- and related -- clues as to what drove large-scale changes to the carbon cycle nearly 100 million years ago. Both research teams conclude that a massive amount of volcanic activity introduced carbon dioxide and sulfur into the atmosphere, which in turn had a significant impact on the carbon cycle, oxygen levels in the oceans and marine plants and animals.

Both teams studied organic carbon-rich sediments from the Western Interior Seaway, an ancient seabed stretching from the Gulf of Mexico to the Arctic Ocean, to learn more about a devastating event 94.5 million years ago when oxygen levels in the oceans dropped so low that one-third of marine life died.

The authors of the first paper, titled "Volcanic triggering of a biogeochemical cascade during Oceanic Anoxic Event 2," reveal that before oxygen levels dropped so precipitously there was a massive increase in

oceanic sulfate levels. Their conclusion is based on analyses of the stable isotopes of sulfur in sedimentary minerals from the central basin of the Western Interior Seaway, located in Colorado.

The researchers theorize that a massive amount of volcanic activity caused this sulfate spike, which triggered a cascade of biogeochemical events. More sulfate led to an abundance of the nutrient phosphorous, which allowed phytoplankton populations in the oceans to multiply. The phytoplankton thrived and then died. Their decomposing bodies depleted oxygen levels in the oceans, leading to the widespread death of marine animals.

The sedimentary burial of marine organic carbon during this event was so large, some prior studies hypothesized that it caused a decrease in atmospheric carbon dioxide levels. In the second Nature Geoscience paper, titled "Carbon sequestration activated by a volcanic carbon dioxide pulse during ocean anoxic event 2," the researchers tested the carbon dioxide drawdown prediction. By studying fossil plant cuticle material, they determined the amount of carbon dioxide in the atmosphere at the time the plants were growing. (The cuticle samples were collected from sites representing the western shore of the Western Interior Seaway, in present-day southwestern Utah.)

This work found that before the onset of ocean anoxia, the level of carbon dioxide in the atmosphere increased by approximately 20 percent. This significant increase is consistent with the volcanic activity invoked by the first Northwestern study (described above). The paleo-carbon dioxide reconstruction also detected two episodes of marked decrease in carbon dioxide levels -- up to 200 parts per million -- at the time of the early phase of marine carbon burial. This observation provides strong support for the carbon dioxide drawdown hypothesis.

"Our research highlights the previously unappreciated role that the sulfur cycle plays in regulating nutrient cycling, the carbon cycle and climate," said Matthew Hurtgen, assistant professor of Earth and planetary sciences in the Weinberg College of Arts and Sciences at Northwestern and lead researcher of the first study.

"These two complementary studies provide a much clearer picture of how the Earth's carbon cycle was dramatically affected by catastrophic natural events long ago," said Bradley Sageman, professor and chair of Earth and planetary sciences at Northwestern and a co-author of both papers. "Although these events played out over hundreds or thousands of years, the magnitude of the changes, in carbon dioxide levels for example, are similar to those of the last 150 years resulting from human influence on the carbon cycle. The evidence demonstrates that the modern carbon cycle has been accelerated by orders of magnitude."

The sulfur work reported in the paper "Volcanic triggering of a biogeochemical cascade during Oceanic Anoxic Event 2" was conducted by Derek D. Adams, a doctoral candidate in Hurtgen's research group. Adams is first author of the paper; Hurtgen and Sageman are the paper's other authors.

Richard S. Barclay, a doctoral candidate in Sageman's research group, is the first author of the "Carbon sequestration activated by a volcanic carbon dioxide pulse during ocean anoxic event 2" paper. Sageman also is an author, and the third author is Jennifer McElwain, a professor from University College Dublin who co-advises Barclay's research and is one of the originators of the cuticle analysis method.

High-fat ketogenic diet to control seizures is safe over long term

Current and former patients treated with the high-fat ketogenic diet to control multiple, daily and severe seizures can be reassured by the news that not only is the diet effective, but it also appears to have no long-lasting side effects, say scientists at Johns Hopkins Children's Center.

A study report supporting their conclusion, and believed to be one of the first analyses of the long-term safety and efficacy of the diet, appears online in the February edition of the journal Epilepsia.

The ketogenic diet, consisting of high-fat foods and very few carbohydrates, is believed to trigger biochemical changes that eliminate seizure-causing short circuits in the brain's signaling system. Used as first-line therapy for infantile spasms and in children whose seizures cannot be controlled with drugs, the diet is highly effective but complicated and sometimes difficult to maintain. It can temporarily raise cholesterol, impair growth and, in rare cases, lead to kidney stones, among other side effects.

"Despite its temporary side effects, we have always suspected that the ketogenic diet is relatively safe long term, and we now have proof," says senior investigator Eric Kossoff, M.D., a pediatric neurologist and director of the ketogenic diet program at Hopkins Children's. "Our study should help put to rest some of the nagging doubts about the long-term safety of the ketogenic diet," he adds.

The evidence is based on a study of 101 patients ages 2 to 26 years treated with the ketogenic diet for a minimum of 16 months and for up to eight years at Hopkins Children's between 1993 and 2008. At the time of the follow-up, patients were off the diet anywhere between eight months and 14 years. Nearly 80 percent of the patients remained either seizure-free or had their seizures reduced by half. Most patients' seizures did not worsen even years after stopping the diet.

Researchers caution it is possible that some effects may not show up for decades. However, the evidence, especially among patients who were off the diet for more than 10 years, suggests no long-term harm.

During interviews, none of the patients reported adverse cardiovascular side effects such as heart attacks, enlargement of the heart or abnormal plaque buildup in their arteries. One patient reported having high blood pressure. Only two of the 101 patients reported kidney stones after stopping the diet, the same rate found in the general population not treated with the ketogenic diet, the researchers say.

None of the 25 patients who had liver and kidney function tests had abnormal results. Among the 26 patients who had their cholesterol tested, the average level was 157 milligrams per deciliter of blood (less than 200 is considered normal), with three of the 26 having abnormal levels. Most patients' cholesterol levels go up while on the diet, but are believed to return to normal thereafter. The Hopkins study now confirms that this is the case.

Most patients older than 18 at the time of the study had normal body mass index of 22 on average (25 and below is considered normal). And most of them were within a few inches of their expected heights, based on their parents' heights. Patients 18 years and younger at the time of the study were, on average, in the 25th percentile for height and in the 36th percentile for weight for their age. While this is below average, the investigators say, it is also much higher than the usual 5th–to-10th percentile while on the diet.

"We have every reason to believe that most children will start catching up once they are off the diet as they grow up because this is what we see in older former patients," Kossoff says.

Contrary to the fear of many parents, the diet does not appear to alter patients' food preferences, the researchers say. Only 8 percent of those in the study said they continued to eat predominantly high-fat foods.

Conflict of interest disclosure: Dr. Kossoff has received grant support from Nutricia, Inc. and consultant fees from Nutricia and Atkins Nutritionals Inc.

The research was funded in part by the National Institutes of Health and the Carson Harris Foundation.

Co-investigators include Amisha Patel, Paula Pyzik, Zahava Turner and James Rubenstein.

New Source of an Isotope in Medicine Is Found

By MATTHEW L. WALD

WASHINGTON — Just as the worldwide shortage of a radioactive isotope used in millions of medical procedures is about to get worse, officials say a new source for the substance has emerged: a nuclear reactor in Poland.

The isotope, technetium 99, is used to measure blood flow in the heart and to help diagnose bone and breast cancers. Almost two-thirds of the world's supply comes from two reactors; one, in Ontario, has been shut for repairs for nine months and is not expected to reopen before April, and the other, in the Netherlands, will close for six months starting Friday.

Radiologists say that as a result of the shortage, their treatment of some patients has had to revert to inferior materials and techniques they stopped using 20 years ago.

But on Wednesday, Covidien, a company in St. Louis that purifies the material created in the reactor and packages it in a form usable by radiologists, will announce that it has signed a contract with the operators of the Maria reactor, near Warsaw, one of the world's most powerful research reactors.

The Maria, a 36-year-old reactor, will fill only a small fraction of the gap left by the shutdowns at Chalk River, Ontario, and Petten, the Netherlands. Still, Dr. Michael M. Graham, a professor of radiology at the University of Iowa and a member of the board of the Society of Nuclear Medicine, said the new arrangement "could make the difference between being able to limp along and shutting down."

As the American base of reactors for research and isotope production withers, the United States has increasingly looked abroad for radioactive materials. The inspector general of the Energy Department has reported that supplies have sometimes been unreliable, either late or not meeting specifications.

But people involved in the transaction said Poland had recently made substantial investments in the Maria reactor, named for the pioneering physicist Marie Sklodowska Curie.

Transferring enriched uranium to a former member of the Soviet bloc and bringing the material back to the Netherlands for processing required 20 permits from five countries, said Stephen E. Littlejohn, a spokesman for Covidien. But the regulatory work is not complete; the Food and Drug Administration will not give permission for the isotope to be used on patients in this country until it has reviewed samples from the new source, Mr. Littlejohn said.

The announcement of the new source for technetium 99 will come amid a flurry of activity around the United States to find new, more reliable ways to make the isotope and to avoid the use of bomb-grade uranium in the process.

General Electric has a plan to make technetium 99 using neutrons from power reactors owned by utilities, a neat trick because those reactors are usually sealed up and run for months at a time, while the medical isotope has to be removed within a few hours of its creation or it decays away. Babcock & Wilcox, a Virginia company that provides a variety of nuclear services, has a plan for a liquid-fueled reactor.

The National Nuclear Security Administration, the Energy Department agency that tries to reduce proliferation, recently said it would help finance both efforts; others are in the works, Obama administration officials say.

The isotope, known as tech 99m, is a product of the rapid decay of another radioactive isotope, molybdenum 99, which is itself produced by splitting atoms of uranium 235. Tech 99m is valued because it emits a gamma ray that is easy to spot in the patient's body. But it, too, decays quickly, so doctors have taken to scheduling procedures late at night and on weekends to make use of material that would otherwise vanish.

Andrzej Strupczewski, chairman of the nuclear safety commission in the Polish Institute of Atomic Energy, said it would be tricky to produce technetium at the Maria reactor because it lacked forced-air systems to cool the uranium that is split to make molybdenum 99. But a recent test went well, he said.

No one seems quite sure whether other reactors can be found to produce the medical isotope. Tammy P. Taylor, a senior policy analyst at the White House Office of Science and Technology Policy, said that while two-thirds of the world's supply came from Petten and Chalk River, "historically, that's more at contractual limits than production and safety limits."

Desmond Tutu leads way for southern African genomes

THE genome club just claimed its first clergyman, in the shape of Archbishop Desmond Tutu. Tutu and a Khoisan man from the Kalahari are the first southern Africans to have their genomes sequenced and published.

In November 2008, a Han Chinese man and a Nigerian man became the first non-whites to have their genomes sequenced. Each of the southern African genomes is a source of further untapped genetic diversity. Interestingly, their genomes are as similar to Europeans' as they are to the other sequenced African genomes - both from Yorubas.

The genome of Tutu, a Bantu, yielded over 412,000 new variants. An even greater number came from the unnamed Khoisan - almost 744,000. This is probably because Khoisans were among the earliest human populations to form and they have not interbred much with other groups, says project leader Stephan Schuster, a genomicist at Pennsylvania State University in University Park (Nature, DOI: 10.1038/nature08795).

Schuster's team say some of the Khoisan's mutations may be down to the group's largely hunter-gatherer lifestyle. Meanwhile, variants lurking in both new genomes may help explain why some southern Africans respond poorly to existing anti-retroviral drugs that treat HIV. If so, this could help design more effective anti-retrovirals, says Schuster.

UC Study Supports Alternative Anti-Seizure Medication Following Acute Brain Injury

CINCINNATI—A study by researchers at the University of Cincinnati Neuroscience Institute (UCNI) at University Hospital supports the use of an alternative medication to prevent seizures in patients who have suffered a life-threatening traumatic brain injury or bleeding stroke.

This randomized study supports earlier indications that the anti-seizure medication levetiracetam, marketed as Keppra, was as effective at preventing seizures as the traditional medication, phenytoin, marketed as Dilantin, while producing fewer negative side effects. Patients treated with Keppra also had improved long-term outcomes, the researchers found. The study will be published in the April 2010 issue of the journal Neurocritical Care; it appeared online on Nov. 7, 2009.

The study of anti-seizure medications in the neuroscience intensive care unit (NSICU) at UC Health University Hospital is part of a focused, ongoing effort to harness scientific evidence to improve treatments and outcomes for patients. Seizures are common following severe brain injury, and minimizing or eliminating them is a primary objective of neurocritical care. The study was led by Lori Shutter, MD, associate professor of neurosurgery and neurology and director of neurocritical care at UCNI. The published article was written by co-investigator Jerzy Szaflarski, MD, PhD, associate professor of neurology.

"We continue to make incremental, meaningful strides in the care of patients who are hospitalized in the NSICU following subarachnoid hemorrhage or traumatic brain injury," Shutter says. (A subarachnoid hemorrhage, a type of bleeding stroke, occurs when blood seeps into the subarachnoid space between the brain and the skull.)

Dilantin has traditionally been the standard of care in preventing seizures, which afflict 25 to 30 percent of patients who have suffered a traumatic brain injury or subarachnoid hemorrhage. Keppra is an established anti-seizure medication given to people with epilepsy (defined as having more than one seizure), but its effectiveness for preventing seizures in patients after a brain injury had not been proven. The study sought to establish the drug's safety and effectiveness in this group of patients.

Although the number of patients in the study was small (52), the results appear to be an indicator that Keppra might be an appropriate alternative to Dilantin for preventing seizures and improving outcomes of patients who have suffered a traumatic brain injury or subarachnoid hemorrhage.

"Preventing seizures is a critical part of protecting a patient's brain from further injury following trauma or stroke," Szaflarski says. Seizures in the neurocritical care setting can result in aneurysm rupture, increased pressure on the brain, oxygen deprivation, physical injury and death. Seizures can be visible (overt), or undetectable to the human eye (covert).

Despite being the standard of care in the neurocritical care setting, Dilantin is linked to many serious and harmful side effects, including medication interactions, rash, fever, low blood pressure, heart arrhythmias, toxicity and organ abnormalities. Previously, the UCNI team, led by Szaflarski, had reported that patients in the NSICU who were treated with Keppra or whose medication was switched to Keppra had fewer complications and shorter hospital stays than those who continued treatment with Dilantin.

This experience led to the newly published study, which compared the safety of Keppra to that of Dilantin and compared the drugs' effect on seizure activity and long-term outcomes. Patients enrolled in the study underwent continuous EEG monitoring for up to 72 hours. EEG, which stands for electroencephalogram, produces a recording of electrical activity in the brain. Two-thirds of the patients were randomly assigned to receive Keppra, while one-third were randomly assigned to receive Dilantin. The physicians were blinded to which medication the patient received.

The results showed that while patients experienced the same outcomes relating to seizure activity and survival, those treated with Keppra suffered fewer side effects and had better long-term outcomes when examined at three- and six-month intervals following their hospital discharge. Shutter notes that the study results had an immediate impact on research protocols for other studies in the NSICU that were not allowing use of Keppra. After this study, the protocols were modified to allow Keppra's use.

Michael Privitera, MD, professor of neurology and director of the UC Epilepsy Center, points to the Keppra study as an example of UCNI's expansion of clinical and research projects associated with the continuous monitoring for seizures in the NSICU. In 2009 more than 200 critically ill patients were monitored in an effort to quantify overt and covert seizures, including life-threatening status epilepticus, a state of continuous brain seizure activity.

"Rapid and accurate detection of seizure activity leads to treatment that can protect nerve cells from damage, especially in cases of subarachnoid hemorrhage or traumatic brain injury," Privitera says. "All of the neurologists and neurointensivists have been trained to perform the initial interpretations of EEG tracings, and our epilepsy staff can verify and read the EEG remotely. University Hospital is the only hospital in the Tristate area with this capability."

The importance of the Keppra study's publication was acknowledged this month, when the article was selected for inclusion in London-based Faculty of 1000 Medicine (www.f1000medicine.com), a literature-awareness service whose mission is to identify and evaluate "the most important articles published in Medicine." Recommendations come from a faculty of more than 2,000 researchers and clinicians.

Jane Hunter, managing director of Faculty of 1000, stated that the article's identification and inclusion provides recognition "of its scientific merit and the positive contribution it makes to the medical literature."

Shutter and Szaflarski have received grant support from UCB Pharma, Inc., the manufacturer of Keppra. Szaflarski has served as a paid consultant and/or speaker for UCB, Inc.

Typos may earn Google $500m a year

* 18:42 17 February 2010 **by Jim Giles**

Google may be earning an alleged $500 million a year via companies and individuals who register deceptive website addresses.

The claim centres on a controversial scheme known as "typosquatting", the practice of registering a misspelled variant of a popular web domain. For example, a typosquatter might register "newscientsist.com" in the hope of getting visits from people who meant to type "newscientist.com".

If that mistake is made frequently enough, the owner of newscientsist.com can profit by placing ads on their page. They could, in particular, use Google's advertising network which automatically assigns ads to a page based on its content, or using keywords provided by the page's owner.

In that case, Google could get a cut too, and Tyler Moore and Benjamin Edelman at Harvard University have now estimated how much money this could bring in for Google

Spelling slips

Moore and Edelman started by using common spelling mistakes to create a list of possible typo domains for the 3264 most popular .com websites, as determined by Alexa.com rankings. They estimate that each of the 3264 top sites is targeted by around 280 typo domains.

They then used software to crawl 285,000 of these 900,000-odd sites to determine what revenue the typo domains might be generating.

If the top 100,000 websites suffer the same typosquatting rate as the sites Moore and Edelman studied, up to 68 million people a day could visit a typo site, they say. They estimate that almost 60 per cent of typo sites could have adverts supplied by Google.

If the company earns as much per visitor from ads on typo sites as it reportedly does from ads alongside search results, it could potentially earn $497 million a year in revenue from typo domains, they conclude.

Google's total 2009 revenues were $23 billion, 97 per cent of which came from advertising.

Removing ads

A Google spokesperson pointed out that the company will remove ads from typo domains if the owner of a site with a trademarked name makes a complaint, but declined to discuss the research in more detail.

Typo domains confuse consumers and can generate unnecessary costs for the owners of the targeted web domain, say Moore and Edelman. Companies can feel compelled to advertise on typo domains targeting their own websites because they fear they might lose business to competitors if they do not.

Edelman has criticised Google's adverts appearing on typo domains in the past. He is currently co-counsel on a lawsuit from a firm seeking damages from Google after its adverts appeared on a typo domain targeting the claimant's website. He says that his involvement in the suit did not influence the results of his research.

Court action

"I'm not doing it for the money," Edelman says of the court action. "I'm doing it because it's important."

Moore and Edelman say their analysis found that some website owners operate thousands of different typo domains. They claim that this means Google and other ad networks would also be able to identify operators of such sites.

A paper on More and Edelman's findings was presented last month at the Financial Cryptography and Data Security conference in Tenerife, Spain. An online appendix provides more information about the analysis.

Jim Giles is a correspondent in New Scientist's San Francisco bureau. He posts at twitter.com/jimgiles

Upside-down answer for deep Earth mystery

Rice scientists: Clues point to 'density trap' in early mantle

HOUSTON - When Earth was young, it exhaled the atmosphere. During a period of intense volcanic activity, lava carried light elements from the planet's molten interior and released them into the sky. However, some light elements got trapped inside the planet. In this week's issue of Nature, a Rice University-based team of scientists is offering a new answer to a longstanding mystery: What caused Earth to hold its last breath?

For some time, scientists have known that a large cache of light elements like helium and argon still reside inside the planet. This has perplexed scientists because such elements tend to escape into the atmosphere during volcanism. However, because these elements are depleted in the Earth's upper mantle, Earth scientists are fairly certain the retained elements lie in a deeper portion of the mantle. Researchers have struggled to explain why some gases would be retained while others would rise and escape into the air. The dominant view has been that the lowermost mantle has been largely isolated from the upper mantle and therefore retains its primordial composition.

In the new study, a team of researchers from Rice, the University of Michigan and the University of California-Berkeley suggests that a particular set of geophysical conditions that existed about 3.5 billion years ago - when Earth's interior was much warmer - led to the formation of a "density trap" about 400 kilometers below the planet's surface. In the trap, a precise combination of heat and pressure led to a geophysical rarity, an area where liquids were denser than solids.

Today, liquids generated in the mantle are less dense than solids and therefore rise to the surface to form volcanoes. However, several billion years ago, a hotter mantle permitted deeper melting and generated dense liquids that stalled, crystallized and eventually sank to the bottom of the mantle.

"When something melts, we expect the gas to get out, and for that reason people have suggested that the trapped elements must be in a primordial reservoir that has never melted," said lead author Cin-Ty Lee, associate professor of Earth scien ce at Rice. "That idea's become problematic in recent decades, because there's evidence that suggests all the mantle should have melted at least once. What we are suggesting is a mechanism where things could have melted but where the gas does not escape because the melted material never rises to the surface."

Lee said the rise of less dense, melted material from Earth's interior is the process that created Earth's crust. Suggesting that melted material might sink instead literally turns conventional wisdom on its head. But the "upside-down" model can explain several geochemical and geophysical oddities in addition to the trapped gases, which suggests that it is a plausible hypothesis. "I hope this generates a lot of interest," Lee said. "There are seismic methods that can be used to test our idea. Even if we turn out to be wrong, the tests that would be needed to falsify our hypothesis would generate a lot of new information."

Research co-authors include Peter Luffi, Tobias Höink and Rajdeep Dasgupta, all of Rice, Michigan's Jie Li and UC-Berkeley's John Hernlund. The research was supported by the Packard Foundation and the National Science Foundation.

UC studies show marijuana has therapeutic value, reports to legislature

First results in United States in 20 years from clinical trials of smoked cannabis

Researchers from the University of California's Center for Medicinal Cannabis Research (CMCR) have found "reasonable evidence that cannabis is a promising treatment" for some specific, pain-related medical conditions. Their findings, presented today to the California legislature and public, are included in a report available on the CMCR web site at http://www.cmcr.ucsd.edu

"We focused on illnesses where current medical treatment does not provide adequate relief or coverage of symptoms," explained CMCR director, Igor Grant, MD, Executive Vice-Chair of the Department of Psychiatry at the UCSD School of Medicine. "These findings provide a strong, science-based context in which policy makers and the public can begin discussing the place of cannabis in medical care."

Researchers have completed five scientific clinical trials, with more in progress. These studies showed that cannabis can be helpful in easing pain in selected syndromes caused by injury or diseases of the nervous system and possibly for painful muscle spasms due to multiple sclerosis.

"These scientists created an unparalleled program of systematic research, focused on science-based answers rather than political or social beliefs," said Senator John Vasconcellos, original author of The Medical Marijuana Research Act of 1999 (SB847) which led to the creation of the CMCR.

Study results have been published in high-impact medical journals, garnering national and international attention which prompted leading experts to come together and foster scientific dialog on the possible uses of cannabis as a therapeutic agent. More study will be necessary to figure out the mechanisms of action and the full therapeutic potential of cannabinoid compounds, according to the UC researchers.

About The Center for Medicinal Cannabis Research:

The CMCR was created in 2000 (through the passage of SB847) to conduct clinical and pre-clinical trials of cannabinoids, including smoked marijuana, to provide evidence, one way or the other, to answer the question "Does marijuana have therapeutic value?" The program's purpose is to oversee objective, high-quality, medical research that would enhance understanding of the efficacy and adverse effects of marijuana as a pharmacological agent. The project was never to be construed as encouraging or sanctioning the social or recreational use of marijuana.

Researchers discover second protective role for tumor-suppressor

DNA damage sensor also responds to oxidative harm outside the nucleus

HOUSTON - ATM, a protein that reacts to DNA damage by ordering repairs or the suicide of the defective cell, plays a similar, previously unknown role in response to oxidative damage outside of the nucleus, researchers report this week in the online version of the Proceedings of the National Academy of Sciences.

"This tumor-suppressor that works in the nucleus to prevent replication of defective cells also has a second life out in the cytoplasm, which was totally unexpected," said senior author Cheryl Walker, Ph.D., professor in The University of Texas M. D. Anderson Cancer Center Department of Carcinogenesis.

"ATM recognizes damage caused by reactive oxygen species (ROS) and tells the cell to stop growing by suppressing the protein-synthesizing pathway mTORC1 or orders the cell to consume itself, a process called autophagy," Walker said. This pathway parallels the protein's role of damage recognition and response in the nucleus.

Reactive oxygen species are a byproduct of cellular metabolism and in small amounts play a role in cell signaling. Their ability to react with other molecules makes them toxic, and they are kept in check by antioxidant enzymes. When that natural balance is disrupted, elevated levels of these volatile molecules damage proteins, lipids and DNA, Walker said. The authors note that elevated ROS has been linked to more than 150 diseases, including diabetes, cancer, neurodegenerative diseases and atherosclerosis.

In its previously known role, ATM (short for ***Ataxia-Telangiectasia Mutated***) senses DNA damage, orders the cell to repair the damage and halts cell division pending repair via the tumor suppressor p53. If repair is not possible, ATM sets off apoptosis - programmed cell death. ATM is commonly mutated in cancer.

The added protective role discovered by the researchers also points to a potential way to activate the tumor-suppressor without damaging DNA.

Walker's lab was studying another tumor-suppressing protein called TSC2 that is active in the cellular cytoplasm and found that ATM appeared to be associated with TSC2 activation.

In a series of experiments, the research team uncovered the molecular pathway that begins with ROS activation of ATM which then:

* Activates the tumor suppressor LKB1, which in turn phosphorylates and activates the AMP kinase (AMPK), a key player in energy sensing and growth factor signaling.

* AMPK switches on the tumor-suppressor TSC2 (tuberous sclerosis complex 2).

* TSC2 then suppresses the kinase mTOR (mammalian Target of Rapamycin), which shuts down the mTORC1 signaling pathway, an important regulator of protein creation and cell growth.

* Because TORC1 suppresses autophagy, when TORC1 is suppressed by TSC2, autophagy is free to occur.

During autophagy, membranes form around organelles in the cytoplasm, which are subsequently digested. Autophagy plays a normal role in cell growth and stability, and is a natural cellular defense mechanism, providing nutrients for a starving cell, for example.

Autophagy also is thought to be a second form of programmed cell death, because it can eventually kill the cell, cannibalizing it and leaving it shot full of cavities. Whether autophagy is activated as a survival mechanism in response to ROS or as an ATM-driven programmed cell death remains to be explored, the authors noted.

Even so, the study links oxidative stress to a key metabolic pathway activated by ATM that integrates damage response pathways with energy signaling, protein synthesis and cell survival.

The study was funded by a variety of grants from the National Institutes of Health, M. D. Anderson Cancer Center, the Children's Hospital Boston Mental Retardation and Developmental Disabilities Research Center and the Sowell-Huggins Fellowship from The University of Texas Graduate School of Biomedical Sciences (GSBS) to co-first author and graduate student Angela Alexander. The GSBS is a joint enterprise of M. D. Anderson and The University of Texas Health Science Center at Houston.

Co-authors with Walker and Alexander are: co-first authors Sheng-Li Cai, Ph.D., Jinhee Kim PhD., and Adrian Nanez, Ph.D., postdoctoral fellows in the Walker lab at the time these studies were performed, Jianjun Shen, Ph.D., and Donna Kusewitt, Ph.D., DVM, all of M. D. Anderson's Department of Carcinogenesis in Smithville, TX; Gordon Mills, M.D., Ph.D., of M. D. Anderson's Department of Systems Biology; Mustafa Sahin, M.D., Ph.D.,of the Department of Neurology at Children's Hospital , Harvard Medical School; Kristeen MacLean and Michael B. Kastan, M.D., Ph.D., of the Department of Oncology at St. Jude Children's Research Hospital in Memphis, Tenn.; Ken Inoki, M.D., Ph.D., of the Life Sciences Institute at the University of Michigan; Kun-Liang Guan, Ph.D., of the Moores Cancer Center at the University of California at San Diego; and Maria Person, Ph.D., of the College of Pharmacy at The University of Texas at Austin.

Sanford-Burnham Scientists Identify Natural Compound that Inhibits Cancer Cell Migration

Molecule found in sea sponges may help control metastasis

LA JOLLA, Calif. - Investigators at Sanford-Burnham Medical Research Institute (Sanford-Burnham, formerly Burnham Institute for Medical Research) led by Kristiina Vuori, M.D., Ph.D., have discovered that the natural compound sceptrin, which is found in marine sponges, reduces cancer cell motility (movement) and has very low toxicity. Metastasis is one of the deadliest aspects of cancer, so restricting aberrant cell movement is an important step towards advancing treatments. The research was published online in ACS Chemical Biology, in collaboration with Phil S. Baran, Ph.D., of The Scripps Research Institute.

The team tested sceptrin in multiple tumor cell types, including cervical, breast and lung cancers. Sceptrin restricted motility in all cell lines. Further tests showed the compound works by limiting the cells' ability to contract, a critical function for cell motility. The researchers also found that sceptrin synthesized in the laboratory was just as effective at combating motility as the naturally-derived compound.

"Given the recently achieved synthesis of sceptrin in multi-gram quantities by the Baran laboratory, sceptrin could prove to be an attractive lead molecule for further preclinical testing and development for therapeutic purposes," said Dr. Vuori. "It may also prove to be a useful research tool in order to elucidate the mechanisms involved in cell motility."

The researchers cultured growing cancer cells with growth factor to encourage motility. These cells were treated with varying amounts of sceptrin, which was found to be more effective at increased concentrations. Subsequently, the team conducted apoptosis and cell proliferation studies to determine whether these mechanisms accounted for the decrease in motility of sceptrin-treated cells. Other assays determined that sceptrin limits motility by reducing cell contractility.

Potentially deadly infection may be linked to frequent cow exposure

EAST LANSING, Mich. — A common bacteria found in many healthy adult females that can cause life-threatening infections when passed to newborns could be introduced to some women through frequent contact with cows, according to a research team led by a Michigan State University pediatrician.

The recently published findings that Group B streptococcus could be a zoonotic disease - transmitted between different species - may have significant public health implications, said Dele Davies, chairperson of MSU's Department of Pediatrics and Human Development.

GBS, first recognized as a bacterium that leads to infections in the breasts of cows, is now found in up to 36 percent of pregnant women in their digestive or genital tracts. When passed to newborns during pregnancy, the infection can be severe - leading to death - though not all infants become sick.

While GBS affects only 1 in every 2,000 babies, and there are prenatal tests to identify it, Davies said understanding how women are infected could greatly reduce transmission rates.

Efforts have been made to understand the risk factors that lead to transmission from mothers to babies, but it hasn't been established how mothers originally acquire it, Davies said.

As part of the study, Davies, fellow MSU professor Shannon Manning and a team of MSU researchers conducted a cross-sectional cohort study of 68 families and their livestock, collecting and comparing stool specimens. Increased frequency of cattle exposure was significantly associated with human infection, and one couple shared the same GBS strains as their cows, suggesting zoonotic transmission.

"Our study suggests that for at least some women, there is an association between increased exposure to cattle and colonization of the bacteria," he said. "Though GBS human infection has long been suspected as originating from cows, several investigators have suggested that ongoing interspecies transmission is unlikely.

"The possibility of ongoing transmission between humans and their livestock has not been systematically examined, and future studies are needed."

The research was published in PLoS One, a journal published by the nonprofit Public Library of Science, at http://www.plosone.org/article/info:doi%2F10.1371%2Fjournal.pone.0008795. Co-collaborators included researchers at MSU's National Food Safety Toxicology Center and the Bureau of Laboratories at the Michigan Department of Community Health.

From Carnivorous Plants to the Medicine Cabinet?

New Tel Aviv University research investigates anti-fungal agents in the sticky "pitchers" of carnivorous plants

In the tropics, carnivorous plants trap unsuspecting prey in a cavity filled with liquid known as a "pitcher."

The moment insects like flies, ants and beetles fall into a pitcher, the plant's enzymes are activated and begin dissolving their new meal, obtaining nutrients such as carbon and nitrogen which are difficult to extract from certain soils. Carnivorous plants also possess a highly developed set of compounds and secondary metabolites to aid in their survival.

These compounds could serve as a new class of anti-fungal drugs for use in human medicine, says Prof. Aviah Zilberstein of Tel Aviv University's Department of Plant Sciences. In a study conducted together with Dr. Haviva Eilenberg from her lab, Prof. Esther Segal from the Sackler Faculty of Medicine and Prof. Shmuel Carmeli from the School of Chemistry, the unusual components from the plants' pitchers were found effective as anti-fungal drugs against human fungal infections widespread in hospitals. The primary results are encouraging.

"To avoid sharing precious food resources with other micro-organisms such as fungi, the carnivorous plant has developed a host of agents that act as natural anti-fungal agents," says Prof. Zilberstein. "In the natural habitat of the tropics, competition for food is fierce, and the hot, moist environment is perfect for fungi, which would also love to eat the plant's insect meal."

Highly resistant and 100% organic

After initial tests of the plant proteins and enzymes that dissolve the chitin of fungi, Prof. Zilberstein assumes that, in the right clinical conditions, the pitcher secondary metabolites can be developed to effective anti-fungal drugs, that may avoid the evolution of new resistant infective strains.

The collaborating team has just published a paper exploring that potential in the Journal of Experimental Biology, based on the biology of the carnivorous plant Nepenthes khasiana. This plant species is originally found in India but is also being reared in Tel Aviv University greenhouses.

Currently there is a need for additional broadly effective anti-fungal drugs. Even mildly severe forms of athlete's foot or other skin fungal infections lack effective treatments. The problem becomes more dire at hospitals, where thousands of Americans die each year from secondary fungal infections they acquire during their stay as patients.

Forging a "wild" pathway in drug discovery

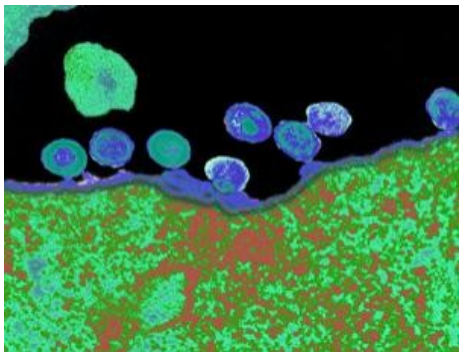
The collaborating team has determined plant secondary metabolites that function as anti-fungal agents. "The pitcher of the carnivorous plant produces these compounds in a gland," says Prof. Zilberstein. Until now, no one has published or discussed the anti-fungal metabolites found in the trap liquid of this plant, she says.

"We're hoping that these metabolites are working together to keep fungus at bay. Our aim now is to get funding for pre-clinical tests of these compounds in an animal model, so we can investigate their effectiveness against the two very acute fungal pathogens found in hospitals worldwide," she says.

The idea that liquid from a plant pitcher could stave off infection has been documented in the folk literature of India, where people drink carnivorous plant pitcher juice as a general elixir. "There is a lot of room for developing compounds from nature into new drugs," says Prof. Zilberstein. "The one we are working on is not toxic to humans. Now we hope to show how this very natural product can be further developed as a means to overcome some basic problems in hospitals all over the world."

Fight HIV with HIV: 'safe' virus proposed as vaccine

* 00:01 19 February 2010 **by Andy Coghlan**



HIV is the cure **(Image: Voisin/Phanie/Rex Features)**

A company is planning to inject people with an HIV vaccine made of the deadly virus itself, albeit a deactivated version. Vaccines against many viruses, including flu, are made from deactivated versions of those viruses, but such an approach was previously dismissed as too risky in the case of HIV.

Now VIRxSYS of Gaithersburg, Maryland, is resurrecting the controversial approach, thanks to successful tests of a similar vaccine against SIV – also known as simian HIV – in monkeys.

"We said 'let's use HIV against itself', and that's what we're doing," says Gary McGarrity, VIRxSYS's vice president of scientific and clinical affairs.

High-profile flop

The idea of turning to the virus itself follows years of frustration with prospective vaccines based on viruses other than HIV, such as adenoviruses that cause colds. Adenoviruses have been modified to carry parts of the HIV virus. Although there were hints of modest success with one such vaccine last year, the previous best bet proved to be a high-profile flop in 2007, during a trial dubbed "STEP".

Crucially, the new tests in monkeys suggest a vaccine based on HIV itself might be more effective than these attempts. The company is planning to apply for approval to perform human trials.

VIRxSYS says such trials would initially be only in people who already carry the virus, rather than in healthy people at risk of infection. This will certainly make for a less controversial trial, as it would avoid any chance of the vaccine going "live" and infecting people who didn't have HIV to start with.

Virus slashed

For now, though, the company's latest results, presented on Thursday at the 2010 annual Conference on Retroviruses and Opportunistic Infections in San Francisco, are limited to a vaccine based on a deactivated version of simian HIV called SIV.

VIRxSYS researchers described how they vaccinated monkeys, and then six months later injected them with SIV. Within weeks of receiving the injection of SIV, concentrations of the virus had fallen by at least 95 per cent in those treated. After a year, when the trial ended, these concentrations remained low, whereas untreated monkeys became progressively sicker as their immune systems were depleted by the virus. "We expect them to die in the next few weeks," says McGarrity.

What's more, in vaccinated animals, concentrations of CD^{4+} cells - the immune cells that both HIV and SIV attack and kill - remained the same, suggesting their immune systems were able to withstand SIV infection.

"These results give us the green light to proceed," says Franck Lemiale of VIRxSYS, who led the two-year trial and presented the results. "We cannot be sure that this will work as well in humans, but this is the point of performing clinical trials.

Entry only

VIRxSYS is convinced that the HIV vaccine it is planning would be safe because, as in their SIV vaccine, all the genes that would usually make it infectious and able to multiply itself would be removed. "It can't replicate," says Lemiale.

All that would be left of the dozen or so genes that HIV normally has would be the three – called gag, pol and rev – that enable it to infiltrate cells and embed itself into their DNA. This means the vaccine's version of the virus only undergoes one cycle of protein production, which enables it to get inside a few cells, but then can't spread further. The hope is that the vaccine version of HIV would invade sentinel cells, known as dendritic cells - as the SIV-based vaccine did in the monkeys. These would then prime the immune system's T-cells to attack the real virus, should it turn up in the body.

Dodge this

The monkey trials also suggested that a vaccine based on HIV itself might be more effective than previous vaccines based on cold viruses.

The "STEP" HIV-vaccine trial had to be halted prematurely in 2007 when it emerged that antibodies produced by the body against the vaccine may have provided HIV with more target cells to infect, speeding its spread.

But VIRxSYS's tests in monkeys revealed that the animals did not produce antibodies against the SIV-based vaccine itself. This suggests that an HIV-based vaccine might dodge the problems that dogged the STEP trial.

Potent mix?

VIRxSYS is not the first company to successfully test SIV-based vaccines in monkeys. A team led by David Evans of Harvard Medical School in Southborough, Massachusetts, reported successfully protecting monkeys a year ago with a similar "single-cycle" vaccine, this time containing all but one of the SIV genes, but he had no intention of transferring the work to people.

There is still the possibility, however, that in people that already have HIV, the vaccine version of the virus could recombine with the incumbent full-strength strain, and evolve into an even more potent adversary.

Evans thinks VIRxSYS has made this less likely by limiting the vaccine virus to a single cycle of infection. "That certainly makes it safer than a replication-competent live attenu8ated virus," he says.

Golden Bough from Roman mythology 'found in Italy'

Italian archaeologists claim to have found a stone enclosure which once protected the legendary "Golden Bough".

By Nick Squires in Rome

In Roman mythology, the bough was a tree branch with golden leaves that enabled the Trojan hero Aeneas to travel through the underworld safely.

They discovered the remains while excavating religious sanctuary built in honour of the goddess Diana near an ancient volcanic lake in the Alban Hills, 20 miles south of Rome.,

They believe the enclosure protected a huge Cypress or oak tree which was sacred to the Latins, a powerful tribe which ruled the region before the rise of the Roman Empire.

The legend inspired JMW Turner to paint a grand canvas entitled 'Lake Avernus - The Fates and the Golden Bough', now held by the Tate Collection

The tree was central to the myth of Aeneas, who was told by a spirit to pluck a branch bearing golden leaves to protect himself when he ventured into Hades to seek counsel from his dead father.

In a second, more historically credible legend, the Latins believed it symbolised the power of their priest-king.

Anyone who broke off a branch, even a fugitive slave, could then challenge the king in a fight to the death. If the king was killed in the battle, the challenger assumed his position as the tribe's leader.

The discovery was made near the town of Nemi by a team led by Filippo Coarelli, a recently retired professor of archaeology at Perugia University. After months of excavations in the volcanic soil, they unearthed the remains of a stone enclosure. Shards of pottery surrounding the site date it to the mid to late Bronze Age, between the 12th and 13th centuries BC.

"We found many, many pottery pieces of a votive or ritual nature," said Prof Coarelli. "The location also tells us that it must have been a sacred structure. We spent months excavating, during which we had to cut into enormous blocks of lava."

The stone enclosure is in the middle of an area which contains the ruins of an immense sanctuary dedicated to Diana, the goddess of hunting, along with the remains of terracing, fountains, cisterns and a nymphaeum.

"It's an intriguing discovery and adds evidence to the fact that this was an extraordinarily important sanctuary," said Prof Christopher Smith, the head of the British School at Rome, an archaeological institute.

"We know that trees were grown in containers at temple sites. The Latins gathered here to worship right up until the founding of the Roman republic in 509BC."

The story about the golden bough and Aeneas, who is said to have journeyed from Troy to Italy to found the city of Rome, was documented by Virgil in his epic, the Aeneid.

"Virgil tells us that the sibyls told Aeneas to go to the underworld to take advice from his father but he had to take a branch of gold as a sort of key to allow him access," said Prof Smith.

The legend inspired JMW Turner to paint a grand canvas entitled 'Lake Avernus – The Fates and the Golden Bough', now held by the Tate Collection.

Dolphins have diabetes off switch

By Victoria Gill Science reporter, BBC News, San Diego

A study in dolphins has revealed genetic clues that could help medical researchers to treat type 2 diabetes.

Scientists from the US National Marine Mammal Foundation said that bottlenose dolphins are resistant to insulin - just like people with diabetes. But in dolphins, they say, this resistance is switched on and off.

The researchers presented the findings at the annual meeting of the American Association for the Advancement of Science (AAAS) in San Diego. They hope to collaborate with diabetes researchers to see if they can find and possibly even control an equivalent human "off switch".

The team, based in San Diego, took blood samples from trained dolphins that "snack" continuously during the day and fast overnight. "The overnight changes in their blood chemistry match the changes in diabetic humans," explained Stephanie Venn-Watson, director of veterinary medicine at the foundation. This means that insulin - the hormone that reduces the level of glucose in the blood - has no effect on the dolphins when they fast.

Big brains

In the morning, when they have their breakfast, they simply switch back into a non-fasting state, said Dr Venn-Watson. In diabetic people, chronic insulin resistance means having to carefully control blood glucose, usually with a diet low in sugar, to avoid a variety of medical complications.

But in dolphins, the resistance appears to be advantageous. Dr Venn-Watson explained that the mammals may have evolved this fasting-feeding switch to cope with a high-protein, low-carbohydrate diet of fish.

"Bottlenose dolphins have large brains that need sugar," Dr Venn-Watson explained. Since their diet is very low in sugar, "it works to their advantage to have a condition that keeps blood sugar in the body… to keep the brain well fed".

But other marine mammals, such as seals, do not have this switch, and Dr Venn-Watson thinks that the "big brain factor" could be what connects human and dolphin blood chemistry.

"We're really looking at two species that have big brains with high demands for blood glucose," she said.

"And we have found changes in dolphins that suggest that [this insulin resistance] could get pushed into a disease state. "If we started feeding dolphins Twinkies, they would have diabetes."

Genetic link

Since both the human genome and the dolphin genome have been sequenced, Dr Venn-Watson hopes to work with medical researchers to turn the discovery in dolphins into an eventual treatment for humans.

"There is no desire to make a dolphin a lab animal," she said. "But the genome has been mapped - so we can compare those genes with human genes."

Scientists at the Salk Institute in San Diego have already discovered a "fasting gene" that is abnormally turned on in people with diabetes, "so maybe this is a smoking gun for a key point to control human diabetes", Dr Venn-Watson said. If scientists can find out what switches the fasting gene on and off in dolphins, they may be able to do the same thing in people.

Lori Schwacke, a scientist from the National Oceanic and Atmospheric Administration (NOAA) in Charleston, South Carolina, said that the work demonstrated that there are interesting similarities between dolphins and humans.

Dr Schwacke, who is studying the effect of pollution on dolphins along the coast of the US state of Georgia, is also interested in the links between dolphin and human health. "There are several interesting diseases that you only see in humans and dolphins," she told BBC News. In this case, Dr Venn-Watson said, "the fundamental difference is that dolphins can switch it off and humans can't".

Giant fish swam prehistoric seas

Prehistoric seas were filled with giant plankton-eating fish which died out at the same time as the dinosaurs, new fossil evidence suggests.

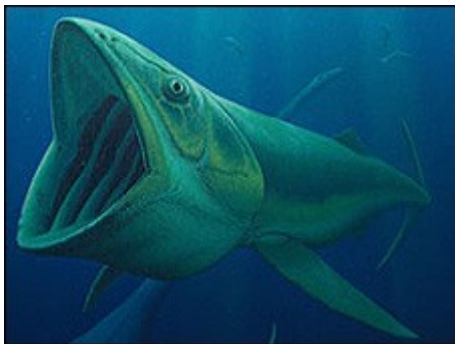
Leedsichthys was a giant filter-feeder in prehistoric oceans

Scientists from Glasgow, Oxford and the United States have identified fossil evidence which shows the fish existed between 66 and 172 million years ago. They believe it may be a "missing piece in the evolutionary story of fish, mammals and ocean ecosystems".

The findings of the research are published in the journal, Science. The international team which carried out the study included academics from Glasgow and Oxford Universities, DePaul University in Chicago, Fort Hays University in Kansas and the University of Kansas.

The project began in Glasgow, with a review of the remains of the giant Jurassic fish Leedsichthys, in conjunction with the excavation of a new specimen of this creature in Peterborough.

Scientists viewed Leedsichthys as an isolated example of a giant filter feeder in the oceans during the age of dinosaurs. But there was a gap in the fossil record between it and the first appearance of modern filter-feeders, some 100 million years later.



Dr Jeff Liston, from Glasgow University, ran the excavation in Peterborough and found the new specimen to be an anomaly. "The breakthrough came when we discovered additional fossils, similar to Leedsichthys, but from much younger rocks," he said.

New fossils

"These specimens indicated that there were giant filter-feeding fishes for much longer than we thought.

"We then started to go back to museum collections, and we began finding suspension-feeding fish fossils from all round the world, often unstudied or misidentified."

Bonnerichthys was identified from a fossil found in Kansas

Several of the most important new fossils - all from the same extinct bony fish family as Leedsichthys - came from sites in Kansas. Other remains originated as far afield as Dorset and Kent in the UK, and in Japan.

Dr Liston added: "The fact that creatures of this kind were missing from the fossil record for over 100 million years seemed peculiar. "What we have demonstrated here is that a long dynasty of giant bony fish filled this space in time for more than 100 million years. "It was only after these fish vanished from the ecosystem that mammals and cartilaginous fish such as manta rays, basking sharks, whale sharks began to adapt to that ecological role." Dr Liston said the findings had "implications for our understanding of biological productivity in modern oceans, and how that productivity has changed over time".

One of the best preserved Kansas specimens had previously been interpreted as similar to a fanged predatory swordfish. When members of the team began to clean the specimen, they found a toothless gaping mouth, with an extensive network of thin elongate bony plates to extract huge quantities of microscopic plankton.

The team named this four to five metre-long fish Bonnerichthys, in honour of the Kansas family who discovered the fossil.

'Koala AIDS' Spreading at an Alarming Rate

By Jennifer Viegas Thu Feb 18, 2010 12:22 PM ET

At least 3.1 million people die of AIDS each year, reports Yale AIDS watch, and scientists have identified a comparable disease, dubbed "Koala AIDS" or "KIDS," which is spreading among the gentle, cuddly marsupials at an alarming rate, according to Australian wildlife health experts.

Although they only live in the wild in Australia, koalas are loved by people all around the world and it's easy to see why!
Photo: Dick Marks, Australian Koala Foundation

Koala Immune Deficiency Syndrome, as the disease is otherwise known, is now documented in the Wildlife Disease Database, maintained by the University of Wisconsin-Madison. It is worrying veterinary scientists who are seeing more and more koala victims of the disease.

"Extinction is inevitable in some areas," Jon Hanger, a veterinary scientist at Australia Zoo's Wildlife Hospital, told CNN. "I certainly hope we don't see it across Australia. But if we don't take the decline seriously and pick up on the warning signs now it's certainly a risk."

Like human AIDS, the disease is not fully understood, but a virus weakens the victim's immune system, leaving the koala vulnerable to cancer, infections and other health problems. The CNN report mentions that KIDS "is spread by koalas coming into contact with each other," suggesting that mating isn't the only possible form of transmission.

Hanger even believes that most koalas carry the virus, but only some are predisposed to it becoming full-blown KIDS. "There is no vaccine available now and may never be," he added, "but what it's saying to us is that we need to be very careful about the way we manage the population. We have to stop destroying habitat and fragmenting it and we've got to address all the causes of death."

According to the Australian Koala Foundation, possibly as few as 43,000 koalas remain in the wild today. In addition to KIDS and habitat loss, koalas face yet another threat: chlamydia.

This sexually transmitted disease can cause infertility, urinary tract infections, and inflammation in the lining of the eye that often leads to blindness, according to professors Peter Timms and Ken Beagley from Queensland University of Technology. Although no vaccine as of yet prevents KIDS, Timms and Beagley have been testing a vaccine for chlamydia in koalas.

"If all goes well with this trial, our future studies will evaluate the vaccine on sick and injured koalas brought in for care, relocated animals, and koalas in other sanctuaries," Timms said in a press release.

"As many as 25-50 per cent of koalas coming into care in both Queensland and NSW (New South Wales) are showing clinical signs of the disease and it seems to be getting worse," he added.

Despite the many serious threats to koalas, and their current population status, Australian officials still refuse to list the marsupials as being "vulnerable," which would provide more protection. If koalas do have a future, I believe it will be thanks to dedicated researchers, possible medical breakthroughs, and tireless human supporters, seen in the following video that also documents the fate of one sick koala.

Fungal Fumes Clear Out Crop Pests

By Jan Suszkiw February 19, 2010

A cocktail of compounds emitted by the beneficial fungus Muscodor albus may offer a biologically based way to fumigate certain crops and rid them of destructive pests. That's the indication from Agricultural Research Service (ARS) studies in which scientists pitted Muscodor against potato tuber moths, apple codling moths and Tilletia fungi that cause bunt diseases in wheat.

The scientists—at ARS laboratories in Aberdeen, Idaho; Wapato, Wash., and other locations—conducted separate studies of Muscodor. However, their goal was the same: to learn whether volatile organic compounds (VOCs) released by the fungus could replace or diminish the use of synthetic pesticides.

In field trials conducted since 2007, ARS plant pathologist Blair Goates found that treating wheat seed or the soil with a formulation of Muscodor and ground rye completely prevented common bunt under moderate disease conditions. Caused by the fungus T. tritici, common bunt reduces wheat yields and grain quality. Although chemical fungicide seed treatments have kept common bunt outbreaks to a minimum, alternative controls are worth exploring if the chemicals lose effectiveness or are discontinued, notes Goates, with the ARS Small Grains and Potato Germplasm Research Unit in Aberdeen. Results from this study were published in the Canadian Journal of Microbiology.

At the ARS Yakima Agricultural Research Laboratory in Wapato, entomologist Lerry Lacey and colleagues tested Muscodor against potato tuber moths, which damage potato leaves and tubers, and apple codling moths, which feed inside apples. In fumigation chamber tests, 85 to 91 percent of adult codling moths died when exposed to Muscodor fumes, while 62 to 71 percent of larvae died or failed to pupate. In apple storage tests, a 14-day exposure to Muscodor killed 100 percent of cocooned codling moth larvae, which are especially difficult to control.

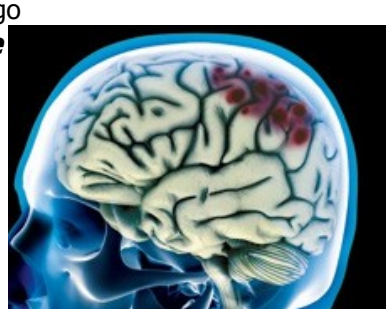
Lacey and colleagues have also been testing Muscodor's effectiveness in biofumigating sealed cartons of apples stored at various temperatures. The results have been encouraging so far, he reports, and there appears to be no adverse effect on the apples' color, firmness or other characteristics.

Read more about this research in the February 2010 issue of Agricultural Research magazine.

Sex hormone trial for head injury

By Victoria Gill Science reporter, BBC News, San Diego

Natural progesterone, the sex hormone used in the first contraceptive pills, is to be tested on patients with severe head injuries.



Progesterone protects neurons in the brain after an injury

Scientists will begin a phase III clinical trial in March and say the drug could save patients' lives and reduce damage to their brains. They announced the trial at the annual meeting of the American Association for the Advancement of Science. It will involve 1,000 patients in 17 trauma centres across the US. Dr David Wright, associate professor of emergency medicine at Emory University in Atlanta, will lead the trial.

Complex condition

Previous studies have shown that progesterone supports the normal development of neurons in the brain, and that the hormone has a protective effect on damaged brain tissue.

Dr Wright told BBC News: "Traumatic brain injury is a complex condition - there's swelling, and neuronal death and damage occurring all at the same time. "The beauty of progesterone is that it seems to work on all of those things."

In earlier tests, the Emory University researchers found that progesterone reduced the risk of death in patients with brain injuries. Dr Wright hopes that, following this trial, progesterone will become the first drug treatment in 30 years to be approved specifically for severe traumatic brain injury.

Yams

The active ingredient, natural progesterone, is very similar to that used in the first contraceptive pills. This has now been superseded by a synthetic progesterone known as progestin. But, for brain injury, only the natural hormone appears to have the desired protective effect.

During the trial, patients with blunt trauma head injuries will be given an infusion of natural progesterone that will last for four days. The hormone is extracted from yams - also known as sweet potatoes.

"The dose is probably about three times what would be found in [the blood] of a female in the third trimester of pregnancy," Dr Wright explained.

The US Food and Drug Administration (FDA) has made a special allowance for the team to administer the drug without patients' consent - so it can be given as soon as possible and have the maximum protective effect.

Neuroscientist: Think twice about cutting music in schools

Music training enhances brainstem sensitivity to speech sounds

EVANSTON, Ill. - At an 11 a.m. press briefing, Saturday, Feb. 20, at the American Association for the Advancement of Science annual meeting, a Northwestern University neuroscientist will argue that music training has profound effects that shape the sensory system and should be a mainstay of K-12 education.

"Playing an instrument may help youngsters better process speech in noisy classrooms and more accurately interpret the nuances of language that are conveyed by subtle changes in the human voice," says Nina Kraus, Hugh Knowles Professor of Neurobiology, Physiology and Communication Sciences at Northwestern University.

"Cash-strapped school districts are making a mistake when they cut music from the K-12 curriculum," says Kraus, director of the Auditory Neuroscience Laboratory in Northwestern's School of Communication.

Kraus will present her own research and the research of other neuroscientists suggesting music education can be an effective strategy in helping typically developing children as well as children with developmental dyslexia or autism more accurately encode speech.

"People's hearing systems are fine-tuned by the experiences they've had with sound throughout their lives," says Kraus. "Music training is not only beneficial for processing music stimuli. We've found that years of music training may also improve how sounds are processed for language and emotion."

Researchers in the Kraus lab provided the first concrete evidence that playing a musical instrument significantly enhances the brainstem's sensitivity to speech sounds. The findings are consistent with other studies they have conducted revealing that anomalies in brainstem sound encoding in some learning disabled children can be improved with auditory training.

The Kraus lab has a unique approach for demonstrating how the nervous system responds to the acoustic properties of speech and music sounds with sub-millisecond precision. The fidelity with which they can access the transformation of the sound waves into brain waves in individual people is a powerful new development.

The neural enhancements seen in individuals with musical training is not just an amplifying or volume knob effect," says Kraus. "Individuals with music training show a selective fine-tuning of relevant aspects of auditory signals."

By comparing brain responses to predictable versus variable sound sequences, Kraus and her colleagues found that an effective or well-tuned sensory system takes advantage of stimulus regularities, such as the sound patterns that distinguish a teacher's voice from competing sounds in a noisy classroom.

They previously found that the ability of the nervous system to utilize acoustic patterns correlates with reading ability and the ability to hear speech in noise. Now they have discovered that the effectiveness of the nervous system to utilize sound patterns is linked to musical ability.

"Playing music engages the ability to extract relevant patterns, such as the sound of one's own instrument, harmonies and rhythms, from the 'soundscape,'" Kraus says. "Not surprisingly, musicians' nervous systems are more effective at utilizing the patterns in music and speech alike."

Studies in Kraus' laboratory indicate that music - a high-order cognitive process - affects automatic processing that occurs early in the processing stream. "The brainstem, an evolutionarily ancient part of the brain, is modified by our experience with sound," says Kraus. "Now we know that music can fundamentally shape our

subcortical sensory circuitry in ways that may enhance everyday tasks, including reading and listening in noise."

At 3:30 p.m., Saturday, Feb. 20, Kraus will present "Cognitive-Sensory Interaction in the Neural Encoding of Music and Speech" as part of a panel on music-language interactions in the brain at the annual meeting of the American Association for the Advancement of Science.

Singing 'rewires' damaged brain

By Victoria Gill Science reporter, BBC News, San Diego

Teaching stroke patients to sing "rewires" their brains, helping them recover their speech, say scientists. By singing, patients use a different area of the brain from the area involved in speech. If a person's "speech centre" is damaged by a stroke, they can learn to use their "singing centre" instead. Researchers presented these findings at the annual meeting of the American Association for the Advancement of Science (AAAS) in San Diego.

An ongoing clinical trial, they said, has shown how the brain responds to this "melodic intonation therapy". Gottfried Schlaug, a neurology professor at Beth Israel Deaconess Medical Center and Harvard Medical School in Boston, US, led the trial.

The therapy is already established as a medical technique. Researchers first used it when it was discovered that stroke patients with brain damage that left them unable to speak were still able to sing.

Professor Schlaug explained that his was the first study to combine this therapy with brain imaging - "to show what is actually going on in the brain" as patients learn to sing their words.

Making connections

Most of the connections between brain areas that control movement and those that control hearing are on the left side of the brain. "But there's a sort of corresponding hole on the right side," said Professor Schlaug. "For some reason, it's not as endowed with these connections, so the left side is used much more in speech. "If you damage the left side, the right side has trouble [fulfilling that role]." But as patients learn to put their words to melodies, the crucial connections form on the right side of their brains.

Previous brain imaging studies have shown that this "singing centre" is overdeveloped in the brains of professional singers. During the therapy sessions, patients are taught to put their words to simple melodies.

Professor Schlaug said that after a single session, a stroke patients who was are not able to form any intelligible words learned to say the phrase "I am thirsty" by combining each syllable with the note of a melody.

The patients are also encouraged to tap out each syllable with their hands. Professor Schlaug said that this seemed to act as an "internal pace-maker" which made the therapy even more effective.

"Music might be an alternative medium to engage parts of the brain that are otherwise not engaged," he said.

Brain sounds

Dr Aniruddh Patel from the Neurosciences Institute in San Diego, said the study was an example of the "explosion in research into music and the brain" over the last decade. "People sometimes ask where in the brain music is processed and the answer is everywhere above the neck," said Dr Patel.

"Music engages huge swathes of the brain - it's not just lighting up a spot in the auditory cortex."

Dr Nina Kraus, a neuroscientist from Northwestern University in Chicago, also studies the effects of music on the brain. In her research, she records the brain's response to music using electrodes on the scalp.

This work has enabled her to "play back" electrical activity from brain cells as they pick up sounds.

"Neurons work with electricity - so if you record the electricity from the brain you can play that back through speakers and hear how the brain deals with sounds," she explained.

Dr Kraus has also discovered that musical training seems to enhance the ability to perform other tasks, such as reading. She said that the insights into how the brain responds to music provided evidence that musical training was an important part of children's education.

A midday nap markedly boosts the brain's learning capacity

Findings suggest that a biphasic sleep schedule not only refreshes the mind, but can make you smarter

If you see a student dozing in the library or a co-worker catching 40 winks in her cubicle, don't roll your eyes. New research from the University of California, Berkeley, shows that an hour's nap can dramatically boost and restore your brain power. Indeed, the findings suggest that a biphasic sleep schedule not only refreshes the mind, but can make you smarter.

Conversely, the more hours we spend awake, the more sluggish our minds become, according to the findings. The results support previous data from the same research team that pulling an all-nighter – a common practice at college during midterms and finals – decreases the ability to cram in new facts by nearly 40 percent, due to a shutdown of brain regions during sleep deprivation.

"Sleep not only rights the wrong of prolonged wakefulness but, at a neurocognitive level, it moves you beyond where you were before you took a nap," said Matthew Walker, an assistant professor of psychology at UC Berkeley and the lead investigator of these studies.

In the recent UC Berkeley sleep study, 39 healthy young adults were divided into two groups – nap and no-nap. At noon, all the participants were subjected to a rigorous learning task intended to tax the hippocampus, a region of the brain that helps store fact-based memories. Both groups performed at comparable levels.

At 2 p.m., the nap group took a 90-minute siesta while the no-nap group stayed awake. Later that day, at 6 p.m., participants performed a new round of learning exercises. Those who remained awake throughout the day became worse at learning. In contrast, those who napped did markedly better and actually improved in their capacity to learn.

These findings reinforce the researchers' hypothesis that sleep is needed to clear the brain's short-term memory storage and make room for new information, said Walker, who is presenting his preliminary findings on Sunday, Feb. 21, at the annual meeting of the American Association of the Advancement of Science (AAAS) in San Diego, Calif.

Since 2007, Walker and other sleep researchers have established that fact-based memories are temporarily stored in the hippocampus before being sent to the brain's prefrontal cortex, which may have more storage space. "It's as though the e-mail inbox in your hippocampus is full and, until you sleep and clear out those fact e-mails, you're not going to receive any more mail. It's just going to bounce until you sleep and move it into another folder," Walker said.

In the latest study, Walker and his team have broken new ground in discovering that this memory- refreshing process occurs when nappers are engaged in a specific stage of sleep. Electroencephalogram tests, which measure electrical activity in the brain, indicated that this refreshing of memory capacity is related to Stage 2 non-REM sleep, which takes place between deep sleep (non-REM) and the dream state known as Rapid Eye Movement (REM). Previously, the purpose of this stage was unclear, but the new results offer evidence as to why humans spend at least half their sleeping hours in Stage 2, non-REM, Walker said.

"I can't imagine Mother Nature would have us spend 50 percent of the night going from one sleep stage to another for no reason," Walker said. "Sleep is sophisticated. It acts locally to give us what we need."

Walker and his team will go on to investigate whether the reduction of sleep experienced by people as they get older is related to the documented decrease in our ability to learn as we age. Finding that link may be helpful in understanding such neurodegenerative conditions as Alzheimer's disease, Walker said.

In addition to Walker, co-investigators of these new findings are UC Berkeley post-doctoral fellow Bryce A. Mander and psychology undergraduate Sangeetha Santhanam.

Some 'Dinosaurs' Evolved from Birds?

By Jennifer Viegas Wed Feb 17, 2010 01:31 PM ET

Some animals identified as being dinosaurs may have evolved from birds, according to a recent paper published in the Proceedings of the National Academy of Sciences.

Creationists are already all over this one.

Keep in mind that animals can evolve similar traits independently. The accepted transition from dinosaur to bird, or in this proposed case—bird to dinosaur—didn't necessary follow a simple path from large beast to tiny, feathered flier. For example, some dinosaurs are thought to have had feathers and beaks, traits we now tend to associate with birds. It's also believed that some dinosaurs increased in size, shrunk, and then became large again. The evolutionary paths, in other words, don't always follow certain, predictable courses, since animals are constantly adapting to ever-changing habitats and climates.

The new PNAS paper doesn't entirely surprise me, because there have been recent discoveries of very bird-like dinosaurs that weren't even very closely related to birds. Check out our story on ***Haplocheirus sollers***, for example. I tend to agree with Jonah Choiniere, lead author of that Science paper, who believes the first birds emerged out of the Maniraptora, aka "hand snatcher," clade, but birds and dinosaurs from that point on then went down different evolutionary paths.

John Ruben, a professor of zoology at Oregon State University, authored a commentary on the PNAS paper. Ruben doesn't dispute that birds and dinosaurs likely shared a common ancestor. Per the study, however, he suggests that once birds started down their own evolutionary path they may have given rise to raptors. This is where the debate heats up because he and others contend that very bird-like 'dinosaurs,' such as Velociraptor, may have actually been more bird than dinosaur.

"Raptors look quite a bit like dinosaurs but they have much more in common with birds than they do with other theropod dinosaurs such as Tyrannosaurus," Ruben said. "We think the evidence is finally showing that

these animals, which are usually considered dinosaurs, were actually descended from birds, not the other way around."

He believes birds, on the other hand, may not have descended from ground-dwelling theropod dinosaurs, but instead from a gliding animal that moved somewhat like a modern day flying squirrel.

"We're finally breaking out of the conventional wisdom of the last 20 years, which insisted that birds evolved from dinosaurs and that the debate is all over and done with," Ruben said. "This issue isn't resolved at all. There are just too many inconsistencies with the idea that birds had dinosaur ancestors, and this newest study adds to that."

(An image drawn in 1915 by naturalist William Beebe suggests a hypothetical view of what early birds may have looked like, gliding down from trees - and it bears a striking similarity to a fossil discovered in 2003 that is raising new doubts about whether birds descended from ground-dwelling theropod dinosaurs. **Photo courtesy of Oregon State University.**

He added, ""Pesky new fossils...sharply at odds with conventional wisdom never seem to cease popping up. Given the vagaries of the fossil record, current notions of near resolution of many of the most basic questions about long-extinct forms should probably be regarded with caution."

Additional information related to the overall topic may be found at this Oregon State University page.

Linchpin of immune system doubles as stroke protector

ANTIBODIES - the linchpin of our natural defences against bacteria and viruses - may also protect us from strokes.

People with low levels of a particular type of antibody tend to have more heart attacks. Now it seems they are also at greater risk of strokes, according to a study of 682 Swedes (Stroke, DOI: 10.1161/strokeaha.109.558742). The antibodies in question target phosphorylcholine, a fat found on the surface of various bacteria and parasites. But they also seem to inhibit the development of the fatty plaques that can clog up blood vessels and cause strokes.

The biggest effect was seen in women: those whose antibody levels were less than 30 per cent of the average had almost a three-fold higher risk of having a stroke. "It's comparable to the risk from high blood pressure," says Johan Frostegård of the Karolinska Institute in Stockholm, Sweden. He led the study and has set up a firm to develop a vaccine and treatments based on artificial antibodies. Women have naturally higher antibody levels, which could help explain their lower rate of strokes and heart attacks, says Frostegård's team.

Enzyme deficiency protects hepatitis C patients from treatment-related anemia

DURHAM, N.C. – Many people who undergo treatment for hepatitis C develop hemolytic anemia, a disorder that destroys red blood cells. In some cases, it is so severe they have to reduce their medication or stop therapy altogether. But now, scientists in Duke University's Institute for Genome Sciences & Policy (IGSP) have discovered two genetic alterations linked to a benign enzyme condition that keep some patients anemia-free.

They say the discovery, appearing online in the journal Nature, opens the door to treatment for patients who have never been considered candidates for therapy before and may also hold the key to new drugs that could prevent anemia from developing in the first place.

The protective mechanism is a deficiency in a gene called ITPA. "We found that patients who carried specific functional variants are strongly protected against developing anemia," says David Goldstein, Ph.D., director of the Center for Human Genome Variation in the IGSP and a senior author of the study.

Previous studies had identified the genetic variants as the cause of a deficiency in the production of an enzyme, inosine triphosphatase. But it was only through a genome-wide association study that the Duke team was able to show that these same variants were protective against anemia induced by ribavirin, one of two necessary drugs in hepatitis C treatment.

About 180 million people world-wide are infected with the hepatitis C virus, and about 30 to 40 percent of them could develop some degree of treatment-related anemia, according to John McHutchison, M.D. associate director for research at the Duke Clinical Research Institute and also a senior author. "It's a big problem. Hemolytic anemia reduces the level of hemoglobin in the blood and robs it of its ability to carry oxygen. Anything that could help us predict who is going to become anemic and who is not could help us better manage therapy and give all patients the best chance of a good outcome."

Goldstein and McHutchison, who had earlier worked together in identifying genetic variants that helped explain race-based differences in response to hepatitis C treatments, believed there was probably a gene-based solution to the anemia puzzle as well.

Working with first authors Jacques Fellay, M.D.; Alex Thompson, M.D., PhD.; and Dongliang Ge, Ph.D., investigators turned to a rich database already at hand: the records of 1286 individuals who had earlier taken part in the IDEAL study, a large, randomized, Duke-led clinical trial that compared leading therapies for hepatitis C. Researchers separated the patients into three ethnic groups, (988 European Americans, 198 African Americans, and 100 Hispanic Americans) and analyzed their decline in hemoglobin levels during the first month of treatment.

The researchers conducted a genome-wide association study and found several polymorphisms - single-letter DNA alterations - also known as "SNPs or "snips" –associated with reduced hemoglobin levels. But finding an association is just a start: of more biological importance is the identification of the causal variants, the polymorphisms that directly influence hemoglobin levels. Investigators discovered that the two variants known to cause ITPA deficiency appeared almost exclusively on chromosomes that also carried the protective version of the most associated SNP. Further statistical analysis proved that the two variants were indeed the source of protection from anemia.

McHutchison says the discovery is clinically important. "The beauty of this finding is that it may mean we could consider offering treatment to patients who have additional problems, like coronary artery disease or kidney disease. Right now, we are generally uncomfortable treating these patients because anemia could make their underlying condition worse. If a test could tell us which patients are not going to become anemic, we could consider treating them."

"Most of us trace the birth of pharmacogenetics to a 1957 paper by Arno Moltulsky who argued that important drug responses may often depend on genetic differences among people that are invisible until an individual takes a certain drug," says Goldstein. "These ITPA variants reflect this classic formulation of pharmacogenetics, and suggest to us that there are many other important variants that can and should be found through the careful genetic analyses of patients' drug responses."

Colleagues from Duke who contributed to the study include Curtis Gumbs, Thomas Urban, Kevin Shianna, Latasha Little and Andrew Muir. Other co-authors include Mark Sulkowski, from Johns Hopkins; and Ping Qiu, Arthur Bertelsen, Mark Watson, Amelia Warner, Clifford Brass and Janice Albrecht, from Schering-Plough Research Institute.

Schering-Plough Research Institute funded the study and has filed a patent application based on the findings. Ten of the study authors, including Goldstein, Thompson, Ge, Fellay, Urban, Shianna and McHutchison, are listed as inventors on the application.

Drugs 'could stop spread of Aids'

Anti-retroviral treatments (ARVs) and universal testing could stop the spread of Aids in South Africa within five years, a top scientist says.

Dr Brian Williams says the cost of giving the drugs to almost six million HIV-positive patients in the country would be $2-3bn per year. Only about 30% get the life-saving drugs, he said, but early detection and treatment would prevent transmission. This, he said, should be complementary to the search for an Aids vaccine. An effective vaccine, he said, was still a long way away. Dr Williams, a leading figure in the field of HIV research, is based at the South African Centre for Epidemiological Modelling and Analysis (Sacema) in Stellenbosch.

Success story

Speaking at at the annual meeting of the American Association for the Advancement of Science (AAAS) in San Diego, he said 30 million people around the world were infected with HIV - with two million dying each year.

"The tragedy is that the disease continues unabated. The only real success story is the development of these extremely effective drugs that keep people alive and reduce their viral load by up to 2,000 times. They become close to non-infectious.

"While the rapid scale-up in the provision of ART in the last five years has exceeded expectations, it has not reduced HIV-transmission and Aids-related TB because it has been given too late in the course of infection."

Dr Williams argued that by the time people started ART, they had infected "most of those that they would have infected anyway". "We've been using drugs to save lives, but not stop the infection," he said. "It's time to look beyond that." He said that if clinical trials started now, all of the HIV positive people in South Africa could be on ARV treatment within five years. Dr Williams said a few clinical trials were already beginning in the US, Canada and sub-Saharan Africa - and he hoped to have the answer "in one or two years".

Kenneth Mayer, professor of medicine at Brown University in the US state of Rhone Island, agreed that treating patients early with ARVs was a matter of "public health".

The US National Institute of Allergy and Infectious Diseases is planning a trial in New York and Washington - in districts that have an HIV positive population at a similar level to African epidemics.

"We need to get answers [from these trials] quickly. That will help us move forward," Dr Williams said.

"We could break the back of the epidemic. If we can do it, I'm confident it will work."