

## The first molybdenite microchip Surpassing the physical limits of silicon

After having revealed the electronic advantages of molybdenite, EPFL researchers have now taken the next definitive step. The Laboratory of Nanoscale Electronics and Structures (LANES) has made a chip, or integrated circuit, confirming that molybdenite can surpass the physical limits of silicon in terms of miniaturization, electricity consumption, and mechanical flexibility.

"We have built an initial prototype, putting from two to six serial transistors in place, and shown that basic binary logic operations were possible, which proves that we can make a larger chip," explains LANES director Andras Kis, who recently published two articles on the subject in the scientific journal ACS Nano.

In early 2011, the lab unveiled the potential of molybdenum disulfide ( $\text{MoS}_2$ ), a relatively abundant, naturally occurring mineral. Its structure and semi-conducting properties make it an ideal material for use in transistors. It can thus compete directly with silicon, the most highly used component in electronics, and on several points it also rivals graphene.

### Three atoms thick

"The main advantage of  $\text{MoS}_2$  is that it allows us to reduce the size of transistors, and thus to further miniaturize them," explains Kis. It has not been possible up to this point to make layers of silicon less than two nanometers thick, because of the risk of initiating a chemical reaction that would oxidize the surface and compromise its electronic properties. Molybdenite, on the other hand, can be worked in layers only three atoms thick, making it possible to build chips that are at least three times smaller. At this scale, the material is still very stable and conduction is easy to control.

### Not as greedy

$\text{MoS}_2$  transistors are also more efficient. "They can be turned on and off much more quickly, and can be put into a more complete standby mode," Kis explains.

Molybdenite is on a par with silicon in terms of its ability to amplify electronic signals, with an output signal that is four times stronger than the incoming signal. This proves that there is "considerable potential for creating more complex chips," Kis says. "With graphene, for example, this amplitude is about 1. Below this threshold, the output voltage would not be sufficient to feed a second, similar chip."

### Built in flexibility

Molybdenite also has mechanical properties that make it interesting as a possible material for use in flexible electronics, such as eventually in the design of flexible sheets of chips. These could, for example, be used to manufacture computers that could be rolled up or devices that could be affixed to the skin.

For more information: Andras Kis, Director of EPFL's Laboratory of Nanoscale Electronics and Structures (LANES) : +41 21 693 39 25, [andras.kis@epfl.ch](mailto:andras.kis@epfl.ch) Articles on the ACS Nano site:  $\text{MoS}_2$  chips: <http://dx.doi.org/10.1021/nn203715c> Mechanical properties of  $\text{MoS}_2$ : <http://dx.doi.org/10.1021/nn203879f>

<http://www.bbc.co.uk/news/science-environment-15735625>

## Antarctic's hidden world revealed

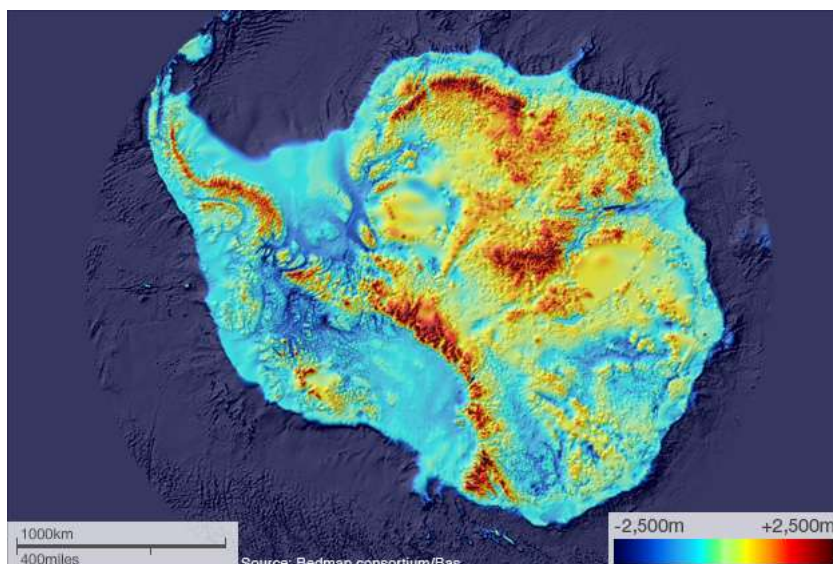
*Ever wondered what Antarctica would look like without all that ice?*

Jonathan Amos By Jonathan Amos Science correspondent, BBC News, San Francisco

Scientists have produced the most detailed map yet of the White Continent's underbelly - its rock bed.

Called simply BEDMAP, this startling view of the landscape beneath the ice incorporates decades of survey data acquired by planes, satellites, ships and even people on dog-drawn sleds. It is remarkable to think that less than 1% of this rock base projects above the continent's frozen veil.

In the map at the top of this page, the highest elevations are marked in red/black. The light blue colour shows the extent of the continental shelf. The lowest elevations are dark blue. You will note the deep troughs within the interior of the continent that are far below today's sea level.



The map is a fascinating perspective but it is more than just a pretty picture - it represents critical knowledge in the quest to understand how Antarctica might respond to a warming world.

Scientists are currently reporting significant changes at the margins of the continent, with increasing volumes of ice now being lost to the ocean, raising global sea levels. The type of information contained in BEDMAP will help researchers forecast the pace of future events.

"This is information that underpins the models we now use to work out how the ice flows across the continent," explained Hamish Pritchard from the British Antarctic Survey (BAS). "The Antarctic ice sheet is constantly supplied by falling snow, and the ice flows down to the coast where great bergs calve into the ocean or it melts. It's a big, slow-speed hydrological cycle. "To model that process requires knowledge of some complex ice physics but also of the bed topography over which the ice is flowing - and that's BEDMAP."

Dr Pritchard is presenting the new imagery on Monday to the 2011 American Geophysical Union (AGU) Fall Meeting, the world's largest annual gathering of Earth and planetary scientists.

This is actually the second generation of the digital BEDMAP. The first version, which was produced in 2001, incorporated 1.9 million measurement points. For BEDMAP2, the sampling has been raised to more than 27 million points on a grid spacing of 5km. "It's like you've brought the whole thing now into sharp focus," Dr Pritchard told BBC News. "In many areas, you can now see the troughs, valleys and mountains as if you were looking at a part of the Earth we're much more used to seeing, exposed to the air."

The source data comes from a range of international partners. Dr Pritchard and BAS colleagues Peter Fretwell and David Vaughan have merged it all into a single product.

The project has benefited greatly from the large number of airborne radar surveys that have been flown in recent years. Unlike rock, ice is transparent to radar. So by firing microwave pulses through the overlying sheet and recording the return echoes, scientists can plot both the depth of the rock bed and - by definition - the thickness of the ice covering. Instrumented planes, guided by GPS, will now fly back and forth across the ice in campaigns that can last weeks at a time.

Perhaps the most publicised of these recent efforts was the multinational expedition in 2007/2008 to map the Gamburtsev mountains. This range is the size of the European Alps with the tallest peaks reaching 3,000m above sea-level - and yet they are still hidden below more than a 1,000m of ice.

"It's fascinating to see the Gamburtsevs in the context of the other big mountains in Antarctica," said Dr Pritchard. "They're similar in size to the likes of the Ellsworth and the Transantarctic mountains, but of course they're completely buried. It is just because the ice is so thick in the middle of the ice sheet that they're not exposed."

It is clear from BEDMAP2 that there are still two big areas of the continent that need improved coverage.

One of these lies between the Gamburtsevs and the coast; the other runs south of the Shackleton mountain range towards the South Pole. Look closely at the map on this page and you can see that the yellow colouring in these areas appears quite smudged. It is very likely that proposals will soon be put to national funding agencies to go and close these data gaps with airborne surveys.

<http://www.scientificamerican.com/article.cfm?id=fda-to-approve-new-generics>

## **FDA to Approve New Generics, But Health Care Savings Will Be Minimal**

***New biological drugs are too complex to be regulated the old way***

**By Sarah Fecht | Monday, December 5, 2011 | 6**

In 1984 the Hatch-Waxman Act made it cheaper and easier to put generic versions of a drug on the market. As a result of the expedited approval process, generics now make up more than 60 percent of prescription drugs sold in the U.S. and have saved the health care system \$734 billion between 1999 and 2008 alone.

By the end of 2011 the FDA plans to release a similar set of guidelines to approve generic versions of biological drugs—a newer breed of pharmaceuticals that includes enzymes, antibodies and other molecules derived from living cells. Unfortunately, experts say, generic versions of biological drugs probably will not be able to reproduce the dramatic savings of the Hatch-Waxman bill.

Biological drugs are used to treat hundreds of types of diseases, including cancer (Herceptin), anemia (Epoen), arthritis (Enbrel), diabetes (Humulin) and human growth disorders (Genotropin). Demand is increasing rapidly for these drugs, even though they tend to be more expensive than traditional synthetic drugs. For example, Cerezyme treatments for a person with a life-threatening enzyme deficiency can cost up to \$500,000 per year, and the cancer drug Avastin costs patients \$100,000 a year. In the U.S., generic versions of these drugs are currently unavailable, at the expense of the patient and the health care system.

Biological generics will be less expensive than brand-name biologicals, says Dominique Gouty, laboratory director for Intertek Pharmaceutical Services, a company that helps pharmaceutical and biotech companies to test drugs, “but they will still be expensive.”

Under the Hatch-Waxman Act, as long as a manufacturer proved its generic drug was chemically identical to the pioneer drug, the generic could piggyback on the pioneer’s clinical research. By avoiding those expensive animal and human trials to assess the drug’s safety and efficacy, generic drugs were able to cut costs by up to 80 percent. Lowering prices will not be so easy for biological generics, however, largely because they will have a harder time avoiding those costly clinical trials. Here’s why:

### **1. Biological drugs are bigger and more complicated than traditional drugs**

A traditional drug such as aspirin is synthesized entirely from precise chemical reactions carried out in a laboratory. Aspirin weighs a relatively light 180 daltons. Getting FDA approval for a generic drug such as this can be almost as simple as supplying the molecular formula. In contrast, interferon beta—an antibody treatment for multiple sclerosis - is harvested from cultures of living cells. It weighs 19,000 daltons and contains complicated folds, twists and carbohydrate attachments. The drug can also come in combination with other cellular proteins.

Tools that would describe and compare these complex features are not fully developed yet. So, whereas analytical tools can tell the FDA whether two proteins have the same amino acid sequence, the higher-order features - folds, twists, carbohydrates and overall shape - largely remain in a black box. And nobody knows how differences in those higher-order features may affect patients taking the drug, Schellekens says.

Stephen Kozlowski, director of the FDA’s biotechnology products office, says that more and better analytical tools will make the approval process for biological generics easier. “We think that if you have a better molecular analysis, it reduces uncertainty about similarity,” he notes. “And if you have more confidence that molecules are structurally and functionally similar, then the number of clinical and animal studies should decrease.”

### **2. Biological drugs depend on touchy manufacturing processes**

Because biological drugs are manufactured in living cells, there can be tremendous variation in the drug molecules produced. Getting exactly the right molecule depends on a precise culturing and extraction process, with very specific environmental conditions. “A one-degree difference in the environment can make the cell react in different ways, and you may have a different drug at the end,” Gouty says. “It’s like if you cut yourself one day, you might bleed for one minute, but for some reason you might bleed for 10 minutes if you cut yourself another day. Living things have lots of variation that we don’t understand and we cannot control.”

When Genzyme attempted to scale up its manufacturing process for Myozyme in 2008, the FDA found that when the process moved from a 160-liter tank to a 2,000-liter tank, the carbohydrate attachments of the enzyme were somehow changed. The company had to repeat its safety and efficacy experiments, and ultimately it had to market the drugs from the larger facility under an entirely new brand name.

“Even within the same company with the same manufacturing process, the product can be different day to day,” Gouty says. A generic manufacturer is likely to have a very different process from the pioneer company, making it even more difficult to create a similar product.

### **3. Biological drugs pose unique safety concerns**

In 2003 Johnson & Johnson learned the hard way that a seemingly small change to the manufacturing process can have devastating consequences. In manufacturing Procrit, a biological treatment for anemia, the company substituted one stabilizing agent for another, which was thought to be safe. Studies later found that 16 percent of Procrit users suffered sudden and sometimes fatal reactions to the drug. After the drug had gone to market, researchers learned that the new stabilizer had unexpectedly reacted with other ingredients, creating substances that caused immunogenic responses and intracranial hemorrhaging in some patients.

Because they are derived from living sources, most biological drugs will be recognized as foreign invaders by the patient’s immune system. It may send antibodies to bind and capture the drug, reducing its efficacy. Sometimes immune reactions to biological drugs can cause fatal side effects, such as organ failure, fever and cancer.

Currently there is no good way to predict how a body will react to a biological drug, says Jeff Mazzeo, a chemist at Waters, a company that designs molecular analysis tools. Bioassays, where a tissue sample in a petri dish is exposed to the drug, “could theoretically tell you how things would act in a biological system,” Mazzeo says. “The problem with bioassays is that they’re extremely variable. They need to be better.”

For these reasons and more, few experts foresee a day when a biological generic could be approved without running clinical trials first. To do so could be irresponsible, Gouty says.

The Federal Trade Commission estimates that generic biological drugs are “unlikely to introduce...discounts any larger than between 10 and 30 percent of the pioneer product’s price.” Nevertheless, those small savings may add up to \$300 billion by 2029, according to some estimates, and future technologies that make it easier to assess the structure and function of a protein could add to those savings. “With enough tools and analysis, my sense is it could be possible to have biosimilars approved with relatively small clinical trials,” Kozlowski says.

At the very least, by encouraging the creation of new versions of biological drugs, the new FDA guidelines will give scientists additional opportunities to study protein structures and the ways they influence safety and effectiveness, Schellekens says. “We’re still in a learning process.”

<http://www.physorg.com/news/2011-12-bacteria-wastewater-chemicals-toxic.html>

### **Bacteria convert wastewater chemicals into toxic form**

***While traces of pharmaceutical compounds are commonly present in wastewater, interactions with bacteria during the treatment process could transform them from non-toxic to toxic forms, a new study suggests.***

PhysOrg.com - Some drugs can occur in two forms, known as enantiomers. While they are chemically very similar, pairs of enantiomers can have drastically different effects on the human body, ranging from medically beneficial to highly toxic.

In cases where both parts are known to be safe, drugs are manufactured and dispensed as mixtures of the two forms. However some drugs are dispensed as single enantiomers since the other form is known to be toxic.

In a study published this month in the journal *Water Research*, UNSW researchers monitored three common pharmaceuticals during wastewater treatment. These included the anti-inflammatory drug naproxen, which is manufactured and dispensed as a single enantiomer, known as S-naproxen. Its counterpart, R-naproxen, is known to be highly toxic to the liver and is not publicly available.

Through the treatment process, researchers observed that some of the safe version of naproxen had been converted to the unsafe form, which could have negative environmental implications. It is the first time that enantiomeric inversion during the wastewater treatment process has been reported.

“We found that some of the S-naproxen had turned into R-naproxen, so even though we’re measuring a major reduction in the concentration of naproxen, the overall toxicity could be increasing,” says study supervisor Dr. Stuart Khan, an environmental engineer at the UNSW Water Research Center.

The process mimics a similar transformation that can be seen in the human gut, where drugs believed to be safe can be inverted during metabolism into their toxic forms.

The most famous case of such inversion is that of thalidomide, a drug designed to control morning sickness that was administered to pregnant women in the late 1950s. Although manufactured as a pure enantiomer, it underwent unexpected inversion in the human gut and caused horrendous birth defects.

Many international studies have reported on the effectiveness of wastewater treatment processes for removing various pharmaceuticals, however, the vast majority of these studies use analytical methods that don’t differentiate between the two enantiomers.

Khan says current eco-toxicological assessments will not be looking for the toxic version of naproxen because it’s not a registered pharmaceutical, so it may not turn up on lists of chemicals requiring assessment.

As a result, assessment will need to be refined and optimised. “We can’t just look at what’s disappearing during the wastewater treatment process, but we need to consider what it’s turning into,” he says. “And is this breakdown product an even greater concern than the original compound?”

It’s not well understood how this transformation is occurring in wastewater, but is believed to be enzyme-driven, says Khan, and is being caused by microorganisms in the treatment plant converting the non-toxic form into the toxic form. Khan and his colleagues are now working to better understand the mechanism of the inversion process and identify other pharmaceuticals for which similar changes may be occurring during wastewater treatment. *Provided by University of New South Wales*

<http://www.physorg.com/news/2011-12-natural-nuclear-reactors-boosted-life.html>

### **Could natural nuclear reactors have boosted life on this and other planets?**

***While modern-day humans use the most advanced engineering to build nuclear reactors, Nature sometimes makes them by accident.***

Evidence for a cluster of natural nuclear reactors has been found on Earth, and some scientists say our planet may have had many more in its ancient past. There’s also reason to think other planets might have had their own naturally occurring nuclear reactors, though evidence to confirm this is hazy. If they did exist, the large amounts of radiation and energy released by such reactors would have had complicated effects on any life developing on this or other worlds, experts say.



Natural nuclear reactors occur when deposits of the radioactive element uranium build up in one spot, and eventually ignite a self-sustaining nuclear chain reaction where uranium divides, in a process called fission, producing other elements. The reaction releases a powerful punch of energy. This energy could prove beneficial and highly detrimental to developing life, depending on the circumstances.

### Only example

The only known examples of natural nuclear reactors on Earth were discovered in the Oklo region of Gabon, Africa, in 1972. French miners discovered that the uranium samples they extracted were depleted in the rare isotope uranium 235, the only naturally occurring material on Earth capable of sustaining fission reactions. It was as if the material had already gone through a nuclear reaction and been used up.

In fact, that's the scenario most supported by studies. Scientists think a concentration of uranium 235 there went critical around 2 billion years ago and underwent fission, just as it does inside man-made nuclear reactors.

"As far as we know, we only have evidence of natural reactors forming and operating at the one site in Gabon, but that demonstrates that it's possible, and our calculations suggest it was much more probable earlier in Earth's history," said Jay Cullen of the University of Victoria in Canada.

Cullen and Laurence A. Coogan, a colleague at the University of Victoria, researched how likely these reactions were when Earth was much younger, based on how much uranium in a given area is necessary for the material to go critical and start a self-sustaining fission reaction. They found that during the Archean epoch, between around 2.5 billion and 4 billion years ago, natural nuclear reactors could have been relatively frequent.

"It certainly seems more than likely that these sorts of reactors would have been much more common in the Earth's early history because the amount [of uranium] you need is actually quite small," Cullen told *Astrobiology Magazine*. However, because there is such a poor geologic record left from so long ago, scientists have very little way of confirming this idea.

### The spark of life

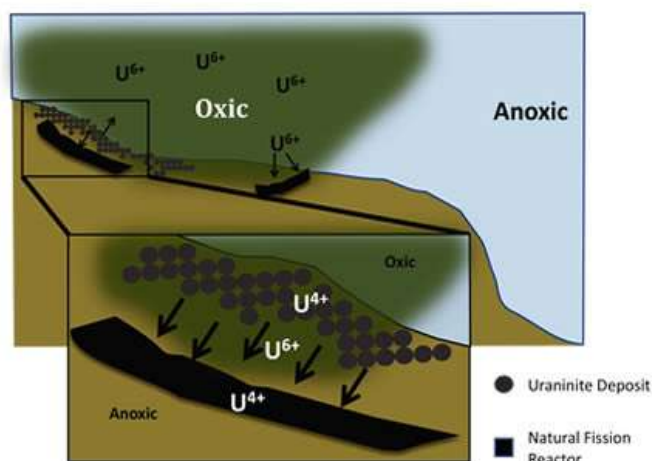
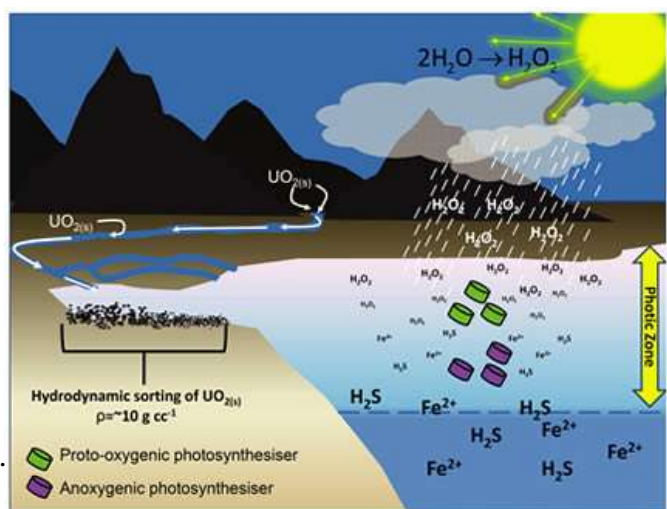
If natural nuclear reactors were present on early Earth, they could have had interesting effects on any nascent life. The ionizing radiation released by a nuclear reaction can damage DNA, the precious instruction code built into every cell of life. If organisms were living too close to the site of a reactor, they could have been wiped out completely. However, life hanging out on the outskirts of a nuclear reactor might have received a smaller dose of radiation — not enough to kill it, but enough to introduce mutations in its genetic code that could have boosted the diversity in the local population.

"The ionizing radiation would actually provide some genetic variation," Cullen said. "That's the quantity that natural selection is going to act upon, and it might help to promote change in organisms with time. I think that most people view ionizing radiation as a bad thing, but that's not always necessarily so."

***This cartoon shows a possible mechanism by which oxygenic photosynthesis could lead to formation of natural fission reactors. Credit: L. A. Coogan/ J. T. Cullen***

Furthermore, the nuclear reactors themselves could have provided an even greater boon to life by giving it the spark it needed to originate in the first place, some scientists think. Zachary Adam, now a graduate student at Montana State University in Bozeman, suggested the possibility in a 2007 paper in the journal *Astrobiology*, which he wrote as a graduate student at the University of Washington.

Scientists don't know for sure how life got started on Earth, but they think it required some kind of burst of energy to start it off. This energy would have been required to break the bonds of simple elements such as carbon, nitrogen, hydrogen and oxygen, so that they could recombine to form the first complex organic molecules.



Other researchers have suggested that a strike of lightning might have provided the requisite energy, but Adam thinks that the energy released by a natural nuclear reactor might have provided the catalyst.

"I think it is at least as possible as other ideas, if not more plausible, but I realize everyone is partial to their own ideas," Adam said.

### **Life elsewhere?**

If natural nuclear reactors might have helped life arise on this planet, it's also possible they've played a role in seeding life elsewhere.

So far, scientists' limited knowledge of the geology of extrasolar planets means they can't say how common natural nuclear reactors might be on other worlds. Adam said that some elements on early Earth that might have helped these reactors form don't seem to be as abundant on the surfaces of other planets.

For example, the Moon's tidal forces on Earth, which used to be stronger than they are today due to the Moon's closer proximity long ago, played a vital role in causing heavy minerals like uranium 235 to collect in dense patches on beaches, Adam said. The Earth had also differentiated into separate layers, including a crust and a mantle, which helped to separate out and concentrate the heavy radioactive elements.

These characteristics, especially crustal differentiation like that on Earth, don't seem to be as common among the other planets of the solar system, Adam said.

But not all experts are pessimistic about natural nuclear reactors on other worlds.

Plasma physicist John Brandenburg of Orbital Technologies Corp. analyzed results from NASA's Mars Odyssey Orbiter, which surveyed the surface of the Red Planet with various instruments, including a gamma-ray spectrometer. Brandenburg says the gamma-ray results show evidence of an abundance of radioactive uranium, thorium and potassium, especially in one particular spot on Mars, which he attributes to a major nuclear reaction taking place there around half a billion years ago.

"Basically it looked as though Mars was covered with a meters-thick layer of radioactive substances, and also the atmosphere was full of radiogenic products," Brandenburg said. "It's kind of a no-brainer at that point. There appears to have been a large radiological event on Mars and it appears to have been violent."

If such a huge nuclear event did occur, it would have been disastrous for any budding Martian life.

"It would have been a terrible catastrophe," Brandenburg said. "Whatever biosphere was on Mars at the time probably suffered a massive extinction event, and it really set back life on Mars."

However, many Mars geologists have greeted Brandenburg's proposal with skepticism.

"This hypothesis is not likely to be true," the University of Arizona's William Boynton, principal investigator for Mars Odyssey's gamma-ray spectrometer, wrote in an email. "Yes, we did find both thorium and uranium, and they are natural elements found everywhere. The amount varies, but the explanations are very mundane."

Boynton said he doubts that natural nuclear reactors like the ones in Gabon are common elsewhere.

"The natural reactor in Africa is real, but the reason it was of so much interest is that it is so rare," Boynton said. "I would say it is all but impossible that any natural reactor has happened anywhere else in the solar system. It may be it has only happened once on Earth!" Source: Astrobio.net

[http://www.eurekalert.org/pub\\_releases/2011-12/uoc--pat120511.php](http://www.eurekalert.org/pub_releases/2011-12/uoc--pat120511.php)

### **Preoperative aspirin therapy can benefit cardiac surgery patients**

#### ***Aspirin taken within five days of cardiac surgery is associated with a significant decrease in the risk of major postoperative complications***

SACRAMENTO, Calif. - Aspirin taken within five days of cardiac surgery is associated with a significant decrease in the risk of major postoperative complications, including renal failure, a lengthy intensive care unit stay and even early death (30-day mortality), according to a study by researchers at Thomas Jefferson University and UC Davis Medical Center set to appear in the journal *Annals of Surgery*.

According to the study's authors, the findings are significant because despite remarkable progress in cardiac surgery, the number of major complications from cardiac surgery remains high.

"Therapies targeted to prevent or reduce major complications associated with cardiac surgery have been few and ineffective so far," said Jianzhong Sun, an anesthesiologist at Thomas Jefferson University and lead author of the study. "These complications are significant and costly both for the public health and the quality of patient life."

The study team evaluated the impact of preoperative aspirin on major outcomes in adults (total 4,256 consecutive patients) who had cardiac surgery -- mostly coronary artery bypass graft or valve surgery -- at Thomas Jefferson University Hospital or UC Davis Medical Center between 2001 and 2009. Among 2,868 patients who met the inclusion criteria, 1,923 took aspirin (about 81 to 325 mg daily) at least once within five days preceding their surgery versus 945 not taking aspirin (non-aspirin therapy).

The outcomes showed that preoperative aspirin therapy (vs. non-aspirin) is associated with a significant decrease in the risk for 30-day mortality, major adverse cardiocerebral events, postoperative renal failure and average time spent in the intensive care unit.

Beneficial effects of preoperative aspirin use found in the current study "are in line with our previous findings and findings from early postoperative aspirin studies," wrote Sun and colleagues in their paper.

"We know that aspirin can be lifesaving for patients who have experienced heart attacks," said Nilas Young, chief of cardiothoracic surgery at UC Davis and a study co-author. "Now we know that this simple intervention can do the same for patients who undergo certain coronary surgeries. This outcome could lead to new preoperative treatment standards in cardiac medicine."

The researchers acknowledge that bleeding remains a concern with preoperative aspirin therapy. However, they said, in the current era of cardiac surgery, the potential for bleeding may be avoided by using antifibrinolytic therapy, which prevents the breakdown of clotting factors in the blood, and/or a low dose of aspirin.

"Overall, the outcome benefits provided by preoperative aspirin therapy may override its possible risk of excess bleeding in patients undergoing cardiac surgery. Nonetheless, further studies are certainly needed to examine this potential side effect carefully," Sun and colleagues wrote.

Added Zvi Grunwald, chair of anesthesiology at Jefferson, "While we are excited that the study clearly showed that preoperative use of aspirin significantly reduced major complications and mortality in patients undergoing cardiac surgery, we do urge further study before recommending aspirin for cardiac surgery patients prior to surgery."

*In addition to Sun and Young, study investigators included senior author Longhui Cao, Scott Silvestry, Will Sun and James Diehl of Thomas Jefferson University; Hong Lui of UC Davis; and Ning Zhao of the University of Pennsylvania Health System.*

<http://www.physorg.com/news/2011-12-oxidative-stress.html>

### **Oxidative stress: Less harmful than suspected?**

#### ***Oxidative stress arises in tissues when there is an excess of what are called reactive oxygen species***

Arterial calcification and coronary heart disease, neurodegenerative diseases such as Parkinson's and Alzheimer's, cancer and even the aging process itself are suspected to be partially caused or accelerated by oxidative stress. Oxidative stress arises in tissues when there is an excess of what are called reactive oxygen species (ROS). "However, up to now, nobody was able to directly observe oxidative changes in a living organism and certainly not how they are connected with disease processes," said Associate Professor (PD) Dr. Tobias Dick of DKFZ. "There were only fairly unspecific or indirect methods of detecting which oxidative processes are really taking place in an organism."

For the first time, Tobias Dick and his co-workers have been able to observe these processes in a living animal. Jointly with Dr. Aurelio Teleman (also of DKFZ), they introduced genes for biosensors into the genetic material of fruit flies. These biosensors are specific for various oxidants and indicate the oxidative status of each cell by emitting a light signal – in realtime, in the whole organism and across the entire life span.

In the fly larvae, the investigators already discovered that oxidants are produced at very differing levels in different tissue types. Thus, blood cells produce considerably more oxidants in their energy plants, the mitochondria, than, for example, intestinal or muscle cells. In addition, the larvae's behavior is reflected in the production of oxidants in individual tissues: The researchers were able to distinguish whether the larvae were eating or moving by the oxidative status of the fat tissue.

Up to now, many scientists have assumed that the aging process is associated with a general increase in oxidants throughout the body. However, this was not confirmed by the observations made by the investigators across the entire life span of the adult animals. They were surprised that almost the only age-dependent increase in oxidants was found in the fly's intestine. Moreover, when comparing flies with different life spans, they found out that the accumulation of oxidants in intestinal tissue even accelerated with a longer life span. The group thus found no evidence supporting the frequently voiced assumption that an organism's life span is limited by the production of harmful oxidants.

Even though comprehensive studies have failed to provide proof until the present day, antioxidants are often advertised as a protection against oxidative stress and, thus, health-promoting. Dick and colleagues fed their flies with N-acetyl cysteine (NAC), a substance which is attributed an antioxidant effect and which some scientists consider suitable for protecting the body against presumably dangerous oxidants. Interestingly, no evidence of a decrease in oxidants was found in the NAC-fed flies. On the contrary, the researchers were



surprised to find that NAC prompted the energy plants of various tissues to significantly increase oxidant production.

"Many things we observed in the flies with the help of the biosensors came as a surprise to us. It seems that many findings obtained in isolated cells cannot simply be transferred to the situation in a living organism," said Tobias Dick, summarizing their findings. "The example of NAC also shows that we are currently not able to predictably influence oxidative processes in a living organism by pharmacology," he adds. "Of course, we cannot simply transfer these findings from fly to man. Our next goal is to use the biosensors to observe oxidative processes in mammals, especially in inflammatory reactions and in the development of tumors."

*More information: Simone C. Albrecht, Ana Gomes Barata, Jörg Großhans, Aurelio A. Teleman and Tobias P. Dick: In vivo mapping of hydrogen peroxide and oxidized glutathione reveals chemical and regional specificity of redox homeostasis. Cell Metabolism 2011, DOI:10.1016/j.cmet.2011.10.010*

*Provided by Helmholtz Association of German Research Centres*

<http://www.physorg.com/news/2011-12-global-tornadoes.html>

### **Global winds could explain record rains, tornadoes**

***Two talks at a scientific conference this week will propose a common root for an enormous deluge in western Tennessee in May 2010, and a historic outbreak of tornadoes centered on Alabama in April 2011.***

Both events seem to be linked to a relatively rare coupling between the polar and the subtropical jet streams, says Jonathan Martin, a University of Wisconsin-Madison professor of atmospheric and oceanic sciences.

But the fascinating part is that the change originates in the western Pacific, about 9,000 miles away from the intense storms in the U.S. midsection, Martin says.

The mechanism that causes the storms originates during spring or fall when organized complexes of tropical thunderstorms over Indonesia push the subtropical jet stream north, causing it to merge with the polar jet stream.

The subtropical jet stream is a high-altitude band of wind that is normally located around 30 degrees north latitude. The polar jet stream is normally hundreds of miles to the north.

Martin calls the resulting band of wind a "superjet."

Jet streams in the northern hemisphere blow from the west at roughly 140 miles per hour, and are surrounded by a circular whirlwind that looks something like a tornado pushed on its side. The circulating wind at the bottom of the jet stream blows from the south. On the north side, the circulating winds turn vertical, lifting and cooling the air until the water vapor condenses and feeds precipitation.

A superjet and its circulating winds carry roughly twice as much energy as a typical jet stream, Martin says. "When these usually separate jet streams sit atop one another, there tends to be a very strong vertical circulation, which produces clouds, precipitation and tornadoes under the right conditions." And because the circulating wind in a superjet moving across the U.S. south picks up moisture from the Gulf of Mexico, "the superjet gives a double-whammy – more moisture, and more lifting, producing that intense rain."

That was the case in May 2010, when 10 to 20 inches of rain fell around Nashville.

Andrew Winters, who is now a graduate student studying with Martin, latched onto the Tennessee flood as the topic of his senior undergraduate thesis in 2010. "It had a lot of interesting aspects, brought an anomalous amount of moisture into the southeast, and that hefty amount of rain," Winters says. And that super-strong jet stream "could be traced back to conditions in the western Pacific, almost a week earlier," Winters says.

Martin and Winters describe their work in talks Dec. 6 and 7 at the annual meeting of the American Geophysical Union in San Francisco.

Studies of the Tennessee floods, the Alabama tornados, and an odd October storm in Wisconsin showed "that when the subtropical jet is pushed poleward under the influence of strong thunderstorms in the western Pacific, it seems to result in these intense storms in the U.S. midsection," Martin says. "It's a really fascinating global connection that occurs seven to 10 days later."

Martin also suggests the altered position of the subtropical jet stream may be linked to global warming.

"There is reason to believe that in a warmer climate, this kind of overlapping of the jet streams that can lead to high-impact weather may be more frequent," Martin says. That idea can be tested, Martin adds.

"Historic weather data should tell us whether there has been a change in the frequency of these overlapping events, and whether that might be linked to a change in high impact-weather events. It's an interesting lead that could help us understand one possible mechanism by which a warmer climate could lead to an increase in severe weather," he says.



Although hurricanes can be tracked for a week or more as they cross the Atlantic Ocean, weather phenomena seldom last so long, Martin says. "If the subtropical jet stream is rearranged and superposed on top of the polar jet stream, it might be the mechanism that allows for this very long delay, a disturbance that can have discernible effect on severe weather thousands of miles downstream, and a week or more later."

Martin says that if the new analysis survives further study, it could contribute to severe weather forecasting. Though severe weather was forecast a day or two in advance of the deadly tornado outbreak in the Southeast this April, "most tornado forecasts are made 12 or at most 24 hours in advance. That saves lives. But if we get the idea five or six days in advance that we should watch the position of the jet streams, we could say, 'Hey, we have a pretty exciting week coming up, we have to be on high alert.'" *Provided by University of Wisconsin-Madison*

<http://www.sciencedaily.com/releases/2011/12/111205165907.htm>

## **Neurotransmitter Dopamine Might Improve the Treatment of Cancer, New Study Suggests**

### ***Doses of a neurotransmitter might offer a way to boost the effectiveness of anticancer drugs and radiation therapy***

ScienceDaily - Doses of a neurotransmitter might offer a way to boost the effectiveness of anticancer drugs and radiation therapy, according to a new study led by researchers at the Ohio State University Comprehensive Cancer Center -- Arthur G. James Cancer Hospital and Richard J. Solove Research Institute.

Using animal models of human breast and prostate cancers, the researchers found that injections of the neurotransmitter dopamine can improve blood flow to tumors and improve delivery of an anticancer drug, doubling the amount of the drug in tumors and increasing its effectiveness. The increased blood flow also raised tumor oxygen levels, a condition that typically improves the effectiveness of both chemotherapy and radiation therapy.

The study also found that dopamine plays an important role in maintaining the structure of normal blood vessels, and that it does this by working through the D2 dopamine receptor, which is present in normal blood-vessel cells called endothelial cells and pericytes. Dopamine was absent in tumor blood-vessel cells.

The findings are published online in the Proceedings of the National Academy of Sciences.

"Our study indicates a use for dopamine in the treatment of cancer and perhaps other disorders in which normalizing abnormal and dysfunctional blood vessels might improve therapeutic responses," says principal investigator Dr. Sujit Basu, associate professor of pathology and a researcher in the OSUCCC -- James Experimental Therapeutics Program.

"Since dopamine and related agents are already used in the clinic for other disorders, these comparatively inexpensive drugs might be applied to the treatment of cancer to increase the therapeutic responses of chemotherapy and radiotherapy," he says.

The blood vessels that develop inside tumors are structurally abnormal, chaotic and leaky and do a poor job of supplying blood to the tumor, Basu notes. This hinders the delivery of chemotherapeutic agents, and it leaves tumors oxygen deprived. This oxygen deprivation makes tumor cells resistant to chemotherapy and radiation.

Basu and his colleagues found that the dopamine treatment normalizes the structure of abnormal tumor blood vessels, indicating an important role for a neurotransmitter in the remodeling of blood vessels. Other key findings include the following:

The tumor tissue used in the study showed the absence of dopamine.

After dopamine treatment, tumor blood vessels in both cases resembled normal vessels in regard to leakiness and architecture. Pretreatment with a dopamine receptor antagonist negated this effect.

Subcutaneous human colon tumors in mice treated with dopamine and the chemotherapeutic drug 5-fluorouracil (5-FU) accumulated twice the amount of 5-FU as tumors in mice treated with the drug only, and the tumors were less than one-third the size of tumors in mice treated with 5-FU only.

"Overall, our findings suggest that the normalization of tumor blood vessels using the neurotransmitter dopamine might be an important approach for improving therapeutic efficacy in the treatment of cancer patients," Basu says.

*Funding from the National Cancer Institute, U.S. Department of Defense Grant mainly supported this research; a grant from the American Heart Association partially supported one of the investigators.*

*The other researchers involved in this study were Debanjan Chakroborty, Chandrani Sarkar, Hongmei Yu, Jiang Wang and Zhongfa Liu of Ohio State University; and Partha Sarathi Dasgupta of Chittaranjan National Cancer Institute, Kolkata, India.*

## **DNA highlights Native American die-off**

***Brief, dramatic population decline after European contact left genetic mark***

**By Bruce Bower**

Genetic evidence now backs up Spanish documents from the 16th century describing smallpox epidemics that decimated Native American populations.

Native American numbers briefly plummeted by about 50 percent around the time European explorers arrived, before rebounding within 200 to 300 years, say geneticist Brendan O’Fallon of ARUP Laboratories in Salt Lake City and anthropologist Lars Fehren-Schmitz of the University of Göttingen in Germany. Population declines occurred throughout North and South America around 500 years ago, the researchers report in a paper published online December 5 in the Proceedings of the National Academy of Sciences.

O’Fallon and Fehren-Schmitz analyzed chemical sequences in ancient and modern mitochondrial DNA, which is inherited from the mother, to calculate the number of breeding females in the Americas over time. Based on those results, O’Fallon estimates that a Native American population of several million fell to roughly half that size once European explorers entered the continent.

“If disease was the primary cause of mortality, surviving Native Americans would have been more resistant to infection after initial epidemics, helping them bounce back quickly,” O’Fallon says.

Researchers disagree about when people first reached the Americas. Whenever initial human settlers arrived, Native American numbers expanded rapidly between 15,000 and 10,000 years ago, several thousand years later than previous DNA-based estimates, the scientists say. Population size then stabilized until suddenly plummeting as the era of European contact dawned, they find.

Several earlier genetic investigations uncovered no signs of mass deaths among Native Americans around the time they first encountered Europeans (SN: 2/16/08, p. 102).

“These new results confirm what’s known from historic sources, but the quality of ancient DNA data raises potential concerns,” remarks geneticist Phillip Endicott of Musée de l’Homme in Paris. An unknown number of chemical sequence changes in mitochondrial DNA preserved in Native Americans’ bones may have resulted from contamination in the ground or after being handled by excavators, Endicott says. These sequence configurations, if intact, provide crucial clues to population trends.

O’Fallon and Fehren-Schmitz analyzed partial sequences of ancient Native American DNA ranging in age from 5,000 to 800 years old. The researchers also examined mitochondrial DNA of 137 people representing five major Native American sequence patterns found in different parts of North and South America.

In the new analysis, only one, relatively rare mitochondrial DNA group repeatedly branched into new genetic lineages over the past 10,000 years. The other four groups display genetic splits bunched within the past few hundred years.

Reasons for these population differences are unclear, O’Fallon says. A closer examination of each of the five Native American genetic groups is needed to confirm that the new estimate of contact-era population losses is accurate, comments anthropological geneticist Connie Mulligan of the University of Florida in Gainesville.

<http://www.sciencedaily.com/releases/2011/12/111205191728.htm>

## **Acupuncture May Ease Severe Nerve Pain Associated With Cancer Treatment, Study Suggests**

***Acupuncture may help ease the severe nerve pain associated with certain cancer drugs***

ScienceDaily (Dec. 5, 2011) - Acupuncture may help ease the severe nerve pain associated with certain cancer drugs, suggests a small preliminary study published in *Acupuncture in Medicine*.

Cancer patients treated with taxanes, vinca alkaloids, or platinum compounds can develop a condition known as chemotherapy induced peripheral neuropathy, or CIPN for short, as a by-product of their treatment. These powerful drugs can damage peripheral nerves, particularly in the calves and feet, which can result in severe nerve pain and/or difficulty walking. As yet, there is no effective antidote.

Out of a total of 192 patients with peripheral neuropathy eligible for inclusion in the study, 11 had developed their symptoms during a course of chemotherapy for various types of cancer. Six of these patients agreed to undergo acupuncture; the other five served as a comparison group.

Twenty needles were inserted at prescribed points and depths and left in place for 20 minutes during each of the 10 sessions. These were delivered over a period of three months by a senior doctor, who had been fully trained in acupuncture and had used the technique for 20 years.

Nerve conduction studies, to assess the signalling speed and intensity of two nerves in the same calf were carried out before acupuncture and again six months after chemotherapy in the six volunteers. The same studies

on patients in the comparison group were carried out after they had completed their chemotherapy and then again six months later. At the second neurological assessment, patients in both groups were asked to state whether they thought their condition had changed or stayed the same.

Clinical examination showed that all the patients had a mixture of numbness on touch and nerve pain, while nerve conduction studies showed evidence of damage to the sural nerve.

In those given acupuncture, both the speed and the intensity of the nerve signalling improved in five out of the six patients. And these same patients said their condition had improved. Among those in the comparison group, speed remained the same in three, fell in one, and improved in one. Intensity remained the same in one, improved in two, and decreased in two.

The authors point to previous research, which suggests that acupuncture may boost blood flow in the legs, which may in turn aid the repair of nerve damage. "The data suggest that acupuncture has a positive effect on CIPN, as measured by objective parameters [nerve conduction studies]," write the authors, adding that their results are similar to those found in patients with nerve damage caused by diabetes and those with peripheral neuropathy of unknown cause. They conclude that the results of this pilot study are "encouraging," and merit further investigation in a larger trial.

<http://bit.ly/u7qa5N>

### **Lab Sabotage: Some Scientists Will Do Anything to Get Ahead**

***In the world of science, it's publish or perish. Less frequently reported are the instances where a desperate scientist resorts to sabotage to take down his or her peers.***

**By Sarah Fecht | December 5, 2011 | Comments3**

In the world of science, it's publish or perish. Researchers who publish a greater number of papers in high-status journals are more likely than their colleagues to win tenure positions, research grants, and prestigious reputations. The competition is fierce enough to compel some scientists to cheat. Anyone who follows the blog Retraction Watch knows that scientists sometimes fudge numbers or plagiarize. Less frequently reported are the instances where a desperate scientist resorts to sabotage to take down his or her peers.

#### **The Lab Rat Shuffle**

Last week, police arrested Mohsen Hosseinkhani for allegedly exacting revenge upon his peers at Mount Sinai Medical Center. The 40-year-old man, upset about losing his fellowship at the hospital, allegedly ran off with \$10,000-worth of hospital property, including stem cell cultures, antibodies, and other scientific materials last July. Before making off with the bounty, Hosseinkhani stopped to shuffle around some lab rats, mixing up control and test rats, apparently out of spite. Hosseinkhani returned to the hospital last week to nick some more pipettes and was taken into custody, as reported in the New York Post.

#### **The Spray-Bottle Betrayal**

In 2009, University of Michigan PhD student Heather Ames began suspecting that someone was tampering with her experiments. Swapped lids on cell cultures, extra antibodies in her western blots, and growth media that were literally drowning in alcohol finally drove Ames to set up two security cameras in the lab. A day later, Ames pulled her cell cultures out of the refrigerator and found that they had again been spiked with alcohol. She reviewed the video footage and watched as her labmate, a post-doctoral student named Vipul Bhrigu, removed his experiments from the refrigerator, then returned with a spray bottle of ethanol and rummaged through the refrigerator for 45 seconds[Video]. The camera couldn't catch what Bhrigu was doing, but at the police station later on, Bhrigu confessed that he had been sabotaging Ames' experiments for months. Bhrigu was ultimately barred from participating in federally-funded research for three years.

#### **The Pilfered Pages**

When biochemist Zhiwen Zhang tried to reproduce the work that earned him a paper in Science in 2004, he discovered that his lab notebooks had gone missing. In 2007, Zhang began receiving anonymous emails from a person who claimed that Zhang's papers had been faked, and threatened to expose Zhang unless he was sent \$4,000 overnight. "They will investigate you," the email said, according to Science Magazine. "Pete will retract all your post-doctoral work. you lose job. ... Texas will fire you before you tenure." Zhang was never able to reproduce his seminal work—in part due to the missing notebooks—and had to retract two of his papers in November 2009.

Such shocking behaviors aren't unique to science—they can occur in any competitive environment, wasting time and money and delaying progress. When sabotage occurs on institutional property, a college or university will typically prosecute according to its Code of Conduct. Unfortunately, researcher anecdotes seem to indicate that, for some reason, many instances of suspected sabotage never get reported in the first place.

[http://www.eurekalert.org/pub\\_releases/2011-12/epfd-bam120211.php](http://www.eurekalert.org/pub_releases/2011-12/epfd-bam120211.php)

## **Bile acids may hold clue to treat heart disease**

***The current study, published supports that theory by demonstrating that a modified bile acid prevents atherosclerosis***

Heart disease is a major cause of death in industrialised countries, and is strongly associated with obesity and diabetes. Many scientists believe that what links these conditions is a chronic, low-grade inflammation. The current study, published in the scientific journal *Cell Metabolism* (December 6, 2011), supports that theory by demonstrating that a modified bile acid called INT-777 prevents atherosclerosis, the build-up of fatty plaques in the walls of arteries, and a leading cause of heart disease—and that it does so by exerting an anti-inflammatory effect.

INT-777 activates a receptor in the membrane of gut cells called TGR5, and in so doing enhances the secretion of a hormone called Glucagon-Like Peptide-1 (GLP-1). GLP-1 is normally induced by feeding, and it stimulates insulin secretion in response to glucose. In earlier work, Profs Kristina Schoonjans and Johan Auwerx of the EPFL's Laboratory of Integrative Systems Physiology (LISP), in collaboration with Prof Roberto Pellicciari of the University of Perugia (Italy) and Intercept Pharmaceuticals (New York, USA), found that they could protect mice fed a high-fat diet from obesity and diabetes by supplementing their food with INT-777.

Anti-diabetic drugs already exist that prolong the activity of GLP-1 in the body. The EPFL group's discovery that INT-777 enhances GLP-1 secretion raised the exciting prospect of combining the two therapeutic approaches for a more effective treatment of diabetes. But how would INT-777 affect any underlying inflammation, and in particular, atherosclerosis?

To find out, LISP members Dr Thijs Pols and Mitsunori Nomura treated mice prone to atherosclerosis with INT-777, and found a significant reduction in plaque formation. Atherosclerotic plaques contain inflammatory cells called macrophages that are generated in the bone marrow. When the bone marrow of the atherosclerosis-prone mice was replaced by bone marrow from either healthy, wild-type mice, or from mice genetically engineered to lack TGR5, the researchers found that only those that received the wild-type marrow showed significantly reduced plaque formation following INT777 treatment. "That was the evidence we needed that it was the anti-inflammatory effect of the compound, acting via TGR5 in bone marrow-derived cells, that accounted for the protective effect," says Dr Schoonjans.

INT777 therefore looks like a promising candidate for the treatment of metabolic syndrome, she says. Unlike some existing anti-diabetes drugs, it is unlikely to have the side-effect of hypoglycaemia, or very low blood glucose, because it only triggers GLP-1 secretion when glucose is in sufficient supply. And though its anti-inflammatory effects are significant, they are moderate, meaning that it would be unlikely to interfere with the normal immune response. The next step will be to devise clinical trials, to test its safety and efficacy in humans.

[http://www.eurekalert.org/pub\\_releases/2011-12/bc-iib120111.php](http://www.eurekalert.org/pub_releases/2011-12/bc-iib120111.php)

## **Inbreeding in bed bugs 1 key to massive increases in infestations**

***As bed bug populations spread throughout the United States, scientists at ASTMH meeting release new research on their biology and behavior***

Philadelphia, Pa.— New research on the bed bug's ability to withstand the genetic bottleneck of inbreeding, announced today at the American Society of Tropical Medicine and Hygiene (ASTMH) annual meeting, provides new clues to explain the rapidly growing problem of bed bugs across the United States and globally. After mostly disappearing in the US in the 1950s, the common bed bug (*Cimex lectularius*) has reappeared with a vengeance over the past decade. These stubborn pests have developed a resistance to the insecticides, known as pyrethroids, commonly used against them.

Scientists at ASTMH also offered new insights into infestations in apartment buildings and homes; a novel approach for preventing insecticide resistance; and new information about chemical compounds involved in attracting and repelling bed bugs.

While these blood-sucking parasites don't transmit disease, their bites provoke allergic reactions—including inflamed welts and severe itching—and they pose both a social and economic threat to owners and residents of apartment buildings, hotels and public buildings. The financial impact has been substantial.

"New York City alone spends between \$10 million and \$40 million per year on bed bug control, and these numbers are repeated in other major cities across the US," noted Rajeev Vaidyanathan, PhD, associate director of Vector Biology and Zoonotic Disease at SRI International. "Over 95 percent of pest control agencies reported bed bugs as a priority in 2010, thus superseding termites as the number one urban pest." The number of reported bed bug infestations in single family homes, hotel rooms and multi-unit housing has increased 10- to 100-fold since those recorded in 1990. Many reasons behind the increases are poorly understood.



One of the newly discovered factors that appears to be contributing to the bed bugs' effective infestation is their ability to establish new infestations through inbreeding. Coby Schal, PhD, and Ed Vargo, PhD, both entomologists at North Carolina State University (NCSU), and colleagues carried out two studies now under peer-review examining the genetics of bed bugs from three multi-story apartment buildings in North Carolina and New Jersey, and determined that there were high levels of relatedness within each apartment and very low genetic diversity within each building, indicating that infestations start from just one or two introductions of the insect. Being able to withstand a very high level of inbreeding—i.e., still produce healthy offspring—allows the bed bug infestation to expand to other apartments within the building.

Another study by this team confirmed this same conclusion based on a study of 21 bed bug infestations from Maine to Florida in the US, nearly all of which came from single rooms within homes. "Inbreeding gives bed bugs an advantage in being able to colonize," said Schal. "A single female that has been mated is able to colonize and start a new infestation. Her progeny and brothers and sisters can then mate with each other, exponentially expanding the population. With many organisms, extensive inbreeding would cause serious mutations that would eventually bring about an end to the population." He also noted that cockroach populations are also able to survive inbreeding.

### **Overcoming Insecticide Resistance**

Further evidence of such resilience has been observed in the bed bugs' resistance to previously successful insecticide strategies. However, new research has revealed that it is possible to "shut down" the mechanism that is linked to breaking down the insecticide and making the bed bug resistant to pyrethroid insecticides.

For the last five years, entomologist Ken Haynes, PhD, and colleagues at the University of Kentucky have been focused on insecticide resistance in bed bugs. He and his colleagues, Subba Reddy Palli and Fang Zhu, looked at a way to eliminate this resistance by targeting specific enzymes inside bed bugs associated with the P450 detoxification system that destroy the insecticides before they reach their molecular target. Rather than attempting to knock out all of the enzymes in the system, the scientists used RNA interference against an enzymatic partner of the P450 family to selectively turn off the system inside bed bugs and preserve the utility of the insecticide—in this case deltamethrin.

### **Building Better Detectors and Traps**

Other potential options for controlling bed bug populations may lie in identifying and understanding the function of chemical compounds secreted by the pests. The researchers revealed that they are still finding new compounds that influence bed bug behavior. Vaidyanathan's group recently isolated seven new compounds that had never been identified from bed bugs that might serve as bed bug attractants. The researchers noted that it might be possible to develop a trap with a "cocktail" of these bed bug compounds to attract the pests.

Mark Feldlaufer, PhD, an entomologist with the US Department of Agriculture's Agricultural Research Service, is working to better understand the underlying mechanisms of the chemical factors, or pheromones that affect bed bug behavior. He has examined the chemical blueprint of "alarm compounds," which warn animals of the same species that there is danger present. These alarm compounds could be used as "dispersants" during a chemical treatment, thereby exposing more bugs to the treatment.

Feldlaufer's research has also recently identified the chemicals associated with the bed bugs' outer skeleton. His focus is now on the role, if any, of these chemicals in the ability of dogs to sniff out bed bugs. When properly trained and handled, canines are used by pest management professionals to find bed bugs just as canines are used to find explosives, drugs or lost people.

### **Bed Bugs and Human Society**

According to Vaidyanathan, "Bed bugs are our oldest roommates. There is even evidence of bed bugs in Pharaonic Egypt."

Researchers say the most recent US resurgence of bed bugs has been caused by a number of factors. "The problems we are seeing with bed bugs in North America did not happen overnight," said Vaidyanathan. "They are the consequence of multiple repeated introductions from all over the world. We have the highest concentration in the history of our species of humans living in cities. For as long as we've been standing on two legs, we've lived in rural areas. Over the last ten years, the majority of humans have moved to urban areas. This is the perfect setting for creating a high density of mammal nests for bed bugs. Bed bugs do not have wings; they are nest parasites, so our own population density has helped them to thrive."

While there is limited genetic diversity within individual infestations, the NCSU team found that there is high genetic diversity across infestations along the East Coast; the bed bugs are coming from many different places, either from within the US or, more likely, from abroad. Previous studies confirm that turnover of residents is one of the biggest indicators for the presence of bed bugs and that increased domestic and

international travel is one of the main factors driving bed bug infestations. Bed bugs also feed on chickens, and industrial production of poultry is providing the perfect breeding grounds for bed bug populations, according to Vaidyanathan. But researchers also attribute the spread to the increased introduction of used furniture and household items into homes.

Right now, either insecticides or heat treatment is used to deal with these infestations. The researchers noted that insecticides readily available to the consumer have generally not been tested against bed bugs. Applying heat treatment involves heating the whole home, or packing all furniture and belongings in a box and heating the objects at a high temperature for one hour, but both are expensive options and not ideal for chronic infestations. The researchers called for better education about bed bugs, improving existing detection methods, and safe and more effective control methods.

"Just as with other global diseases once thought under control and then neglected, bed bugs have shown the ability to resurge in great numbers once our vigilance wanes," said Peter J. Hotez, MD, PhD, president of ASTMH. "To stay one step ahead of bed bugs and other parasitic organisms, we need to sustain investment in research for new tools."

<http://www.scientificamerican.com/article.cfm?id=swapping-germs>

## **Swapping Germs: Should Fecal Transplants Become Routine for Debilitating Diarrhea? A potentially beneficial but unusual treatment for serious intestinal ailments may fall victim to regulatory difficulties**

**By Maryn McKenna | Tuesday, December 6, 2011 | 17**

Marion Browning of North Providence, R.I., was at her wit's end. The 79-year-old retired nurse had suffered from chronic diarrhea for almost a year. It began after doctors prescribed antibiotics to treat her diverticulitis, a painful infection of small pouches in the wall of the colon. The regimen also killed friendly bacteria that lived in Browning's intestines, allowing a toxin-producing organism known as *Clostridium difficile* to take over and begin eating away at the entire lining of her gut.

For months Browning was in and out of her doctor's office, getting big-gun antibiotics to suppress the *C. difficile* infection. Each time a course of treatment ended she would feel better for a while. But her strain of *C. difficile* was stubborn: a few of the destructive bacteria always survived. Within a few days they would begin multiplying, and the racking diarrhea would recur. After four rounds of antibiotics, her gastroenterologist told her that he had done all he could think of. He recommended that she see Colleen Kelly, a clinical faculty member at Brown University's medical school, who was trying something new.

Kelly proposed a treatment that sounded both logical and strangely unmedical. Normally, she told Browning, the friendly bacteria that reside in the human intestine maintain a seesawing balance that keeps pathogenic bacteria in check. That equilibrium can be temporarily disrupted—as with standard antibiotic treatment—but it nearly always returns to stability. Browning's own bacterial community had lost that ability, probably for good. Still, there was a way to restore normality, Kelly said. She could replace Browning's bacteria completely, by inserting into her colon a diluted sample of stool from someone whose intestinal health was good. If the good bacteria in the donated stool took hold and recolonized her intestine, the *C. difficile* would be crowded out, and she would be cured.

Browning had never heard of such a procedure—variously called fecal transplant, fecal bacteriotherapy or fecal flora reconstitution—but she was ready to try anything. Kelly asked her to recruit a healthy donor. Browning chose her 49-year-old son. In the fall of 2009 Browning performed the bowel-cleansing routine that precedes a colonoscopy, while her son took an overnight laxative. Kelly diluted the donation, then used colonoscopy instruments to squirt the solution high up in Browning's large intestine. The diarrhea resolved in two days and has never recurred. "I can't understand why more doctors aren't doing this," says Browning, now 80. Yet a complex combination of federal regulations and research rules—along with just plain squeamishness—could keep the procedure from helping potentially thousands of people who might benefit.

### **A Growing Threat**

Browning is not alone in being a success story. In medical journals, about a dozen clinicians in the U.S., Europe and Australia have described performing fecal transplants on about 300 *C. difficile* patients so far. More than 90 percent of those patients recovered completely, an unheard-of proportion. "There is no drug, for anything, that gets to 95 percent," Kelly says. Plus, "it is cheap and it is safe," says Lawrence Brandt, a professor of medicine and surgery at the Albert Einstein College of Medicine, who has been performing the procedure since 1999.

So far, though, fecal transplants remain a niche therapy, practiced only by gastroenterologists who work for broad-minded institutions and who have overcome the ick factor. To become widely accepted, recommended

by professional societies and reimbursed by insurers, the transplants will need to be rigorously studied in a randomized clinical trial, in which people taking a treatment are assessed alongside people who are not. Kelly and several others have drafted a trial design to submit to the National Institutes of Health for grant funding. Yet an unexpected obstacle stands in their way: before the NIH approves any trial, the substance being studied must be granted “investigational” status by the Food and Drug Administration. The main categories under which the FDA considers things to be investigated are drugs, devices, and biological products such as vaccines and tissues. Feces simply do not fit into any of those categories.

The physicians performing the transplants decry the regulatory bottleneck because new treatments for *C. difficile* infection are critically needed. *C. diff*, to use the common medical shorthand, has risen in the past 30 years from a recognized but tolerated consequence of antibiotic treatment to a serious health threat. Since 2000, when a virulent new strain emerged, cases have become much more common, occurring not only in the elderly but in children, pregnant women and people with no obvious health risks. One study estimated that the number of hospitalized adults with *C. diff* more than doubled from about 134,000 patients in 2000 to 291,000 patients in 2005. A second study showed that the overall death rate from *C. diff* had jumped fourfold, from 5.7 deaths per million in the general population in 1999 to 23.7 deaths per million in 2004.

*C. diff* has also become harder to cure. Thanks to increasing antibiotic resistance, standard treatment now relies on two drugs: metronidazole (Flagyl) and vancomycin. Both medications are so-called broad-spectrum antibiotics, meaning that they work against a wide variety of bacteria. Thus, when they are given to kill *C. diff* infection, they kill most of the gut’s friendly bacteria as well. The living space that those bacteria once occupied then becomes available for any *C. diff* organisms that survive the drugs’ attack. As a result, roughly 20 percent of patients who have had one episode of *C. diff* infection will have a recurrence; 40 percent of those with one recurrence will have another; and 60 percent of those who experience a second bout are likely to suffer several more. Some victims with no other options must have their colon removed. (A new drug, fidaxomicin, which was approved for *C. diff* infection by the FDA in late May, may lead to fewer relapses because it is a narrow-spectrum antibiotic.)

### **A Simple Procedure**

The details of how the transplantation of microbes eliminates *C. diff* infection have not been well studied, but Alex Khoruts, a gastroenterologist and immunologist at the University of Minnesota who has performed two dozen fecal transplants over the past two years, has demonstrated that the transplanted bacteria do take over the gut, replacing the absent friendly bacteria and outcompeting *C. diff*. In 2010 he analyzed the genetic makeup of the gut flora of a 61-year-old woman so disabled by recurrent *C. diff* that she was wearing diapers and was confined to a wheelchair. His results showed that before the procedure, in which the woman received a fecal sample from her husband, she harbored none of the bacteria whose presence would signal a healthy intestinal environment. After the transplant—and her complete recovery—the bacterial contents of her gut were not only normal but were identical to that of her husband.

Most clinicians who perform fecal transplants ask their patients to find their own donors and prefer that they be a child, sibling, parent or spouse. “For me, it’s aesthetic,” says Christina Surawicz, a professor of medicine at the University of Washington, who has done transplants on two dozen patients and published an account of the first 19. “There’s something very intimate about putting someone else’s stool in your colon, and you are already intimate with a spouse.”

To ensure safety, the physicians performing the procedure require that donors have no digestive diseases and put them through the same level of screening that blood donation would require. That process imposes a cost in time and logistics because standard rules for medical confidentiality require a donor to be interviewed separately from the potential recipient. It also carries inherent financial penalties. The donor’s lab work most likely will not be covered by insurance; the transplant procedure may or may not be covered by the patient’s insurance.

Proponents have come up with work-arounds for those possible barriers. Khoruts no longer uses related donors—which requires finding a different individual for every case—but instead has recruited a cadre of “universal donors” from among local health care workers. (He has seen no change in how often the transplants “take.”) Last year Michael Silverman of the University of Toronto boldly proposed a yet more streamlined solution: having patients perform the transplants at home with a drugstore enema kit. A drawback, he cautioned in *Clinical Gastroenterology and Hepatology*, is that too much of the stool solution might leak out for the transplant to take. Nevertheless, seven patients with recurrent *C. diff* have safely performed the home version, he wrote, with a 100 percent recovery rate.

<http://medicalxpress.com/news/2011-12-team-tumor-destruction-method-immunity.html>

## **Team develops tumor destruction method that also creates immunity**

**Researchers at Tel Aviv University are strengthening the odds in favor of permanent tumor destruction**

Even when surgical tumor removal is combined with a heavy dose of chemotherapy or radiation, there's no guarantee that the cancer will not return. Now researchers at Tel Aviv University are strengthening the odds in favor of permanent tumor destruction - and an immunity to the cancer's return - with a new method of tumor removal.

Based on "tumor ablation," a process through which the tumor is destroyed inside the body, Prof. Yona Keisari of TAU's Sackler Faculty of Medicine and Prof. Itzhak Kelson of TAU's Department of Physics and Astronomy have developed a radioactive wire, less than an inch long and about the width of a pin. When inserted into a solid tumor, the wire releases lethal radioactive atoms that irradiate the tumor from the inside out.

As it breaks down, the tumor releases antigens which trigger an immune response against the cancerous cells, Prof. Keisari explains. Not only are cancerous cells more reliably destroyed, but in the majority of cases the body develops immunity against the return of the tumor, a rare happening when the tumor is removed surgically.

The research has been published in a number of academic journals, most recently Translational Research.

### **A cancer-fighting cluster bomb**

Currently, cancer patients receive gamma radiation when they undergo radiation therapy. Although alpha particles are much more effective, their range is so short that they're unable to penetrate the skin, and therefore ineffective in traditional radiation treatments. As developed in Prof. Kelson's lab, the radioactive wire circumvents the drawbacks of alpha radiation by implanting radioactive ions directly into the tumor.

"The wire is coated in atoms that emit not just alpha particles, but also daughter atoms which are themselves alpha emitters. These particles diffuse inside the tumor, spreading further and further before disintegrating," Prof. Kelson explains. "It's like a cluster bomb — instead of detonating at one point, the atoms continuously disperse and emit alpha particles at increasing distances." The process takes approximately ten days, leaving only non-radioactive and non-toxic amounts of lead. The wire itself, which is initially inserted into the tumor by hypodermic needle, decays harmlessly in the body.

In pre-clinical trials on mouse models, this method has shown a distinct advantage over surgical tumor removal. One group of the mice was treated with surgical tumor removal, while another group underwent ablation treatment using the radioactive wire. When cells from the tumor were re-injected into the subject, 100 percent of those treated surgically redeveloped their tumor, compared to only 50 percent of those treated with the radioactive wire. The researchers have had excellent results with many types of cancer models, including lung, pancreatic, colon, breast, and brain tumors.

Ultimately, this shows that tumor removal by ablation increases immunity against the return of the cancerous tumor cells. "Surgery can eliminate 80 to 90 percent of a tumor, chemotherapy another 5-15 percent," says Prof. Keisari. "There are often a small number of metastatic cells left in the body, and they kill about 85% of the patients." Ablation methods, through the stimulation of specific anti-tumor immunity, have a better record for killing off the cancer cells that escape other types of treatment. It's also less invasive, more efficient, and more cost-effective.

### **Technology heads to trial**

The treatment, called D $\alpha$ RT (Diffusing Alpha-emitters Radiation Therapy), has now been commercialized by Althera Medical Ltd., co-located in Tel Aviv and New York City, and will soon undergo clinical trials at Beilinson Hospital in Israel. According to Prof. Keisari, this is just the beginning of an emerging field of cancer treatment. He hopes to see researchers from all over the world come together to create a comprehensive view of the advances in tumor ablation and the stimulation of anti-tumor immunity. In collaboration with Prof. Rafi Korenstein, also of the Sackler Faculty of Medicine, Prof. Keisari has developed a second ablation technique, called pulsed electric current ablation, in which electrodes are inserted into tumors and emit electrical currents to create a chemical reaction that destroys the tumor. *Provided by Tel Aviv University*

<http://www.sciencedaily.com/releases/2011/12/111206131404.htm>

## **New Tick-Borne Disease Discovered in Sweden**

**Researchers have discovered a brand new tick-borne infection**

ScienceDaily - Researchers at the University of Gothenburg's Sahlgrenska Academy have discovered a brand new tick-borne infection. Since the discovery, eight cases have been described around the world, three of them in the Gothenburg area, Sweden.



In July 2009 a 77-year-old man from western Sweden was out kayaking when he went down with acute diarrhea, fever and temporary loss of consciousness. He was taken to hospital where it was found that he was also suffering with deep vein thrombosis (DVT). Following treatment with antibiotics, he was discharged some days later with an anticoagulant to thin his blood. However, the man - who had an impaired immune system - went down with a fever again.

### **Brand new infection**

Over the following months the 77-year-old was admitted as an emergency case on several occasions, but despite repeated attempts to find a microbe, and repeated doses of antibiotics, the fever returned. Finally the patient's blood underwent special analysis to look for bacterial DNA -- and that produced results. The findings matched a bacterium in an online gene bank and the results were a sensation: the man had contracted a brand new infection in humans which had never been described in the world before.

### **Never before seen in Sweden**

The man's blood contained DNA that derived with 100% certainty from the bacterium *Neoehrlichia mikurensis*. This bacterium was identified for the first time in Japan in 2004 in rats and ticks but had never before been seen in Sweden in ticks, rodents or humans.

Christine Wennerås, a doctor and researcher at the Department of Infectious Diseases and the Department of Haematology and Coagulation at the University of Gothenburg's Sahlgrenska Academy, has been studying the case since it first came to light. Last year she was able, for the first time, to describe the newly discovered disease in a scientific article published in the *Journal of Clinical Microbiology*. "Since our discovery the bacterium has been reported in eight cases around the world, three of them in Gothenburg," says Wennerås.

### **Causes DVT**

All three of the Gothenburg cases involved patients with an impaired immune system, all of whom became ill during the summer months when ticks are most active. "The nasty thing about this infection is that it causes DVT, at least in people with an impaired immune system," says Wennerås. "This can be life-threatening. Fortunately, the infection can be treated successfully with antibiotics.

### **Spreads from mammals**

"If the newly discovered bacterium is similar to those we already know, it has presumably spread from wild mammals to people via ticks, and it is unlikely that it can be passed on from person to person."

The *mikurensis* in the bacterium's name comes from the Japanese island of Mikura, where it was first discovered.

[http://www.eurekalert.org/pub\\_releases/2011-12/sfn-dra120711.php](http://www.eurekalert.org/pub_releases/2011-12/sfn-dra120711.php)

### **Drug reverses aging-associated changes in brain cells**

#### ***Animal study offers insights into possible drug targets to improve memory as we age***

Washington, DC -- Drugs that affect the levels of an important brain protein involved in learning and memory reverse cellular changes in the brain seen during aging, according to an animal study in the December 7 issue of *The Journal of Neuroscience*. The findings could one day aid in the development of new drugs that enhance cognitive function in older adults.

Aging-related memory loss is associated with the gradual deterioration of the structure and function of synapses (the connections between brain cells) in brain regions critical to learning and memory, such as the hippocampus. Recent studies suggested that histone acetylation, a chemical process that controls whether genes are turned on, affects this process. Specifically, it affects brain cells' ability to alter the strength and structure of their connections for information storage, a process known as synaptic plasticity, which is a cellular signature of memory.

In the current study, Cui-Wei Xie, PhD, of the University of California, Los Angeles, and colleagues found that compared with younger rats, hippocampi from older rats have less brain-derived neurotrophic factor (BDNF) — a protein that promotes synaptic plasticity — and less histone acetylation of the *Bdnf* gene. By treating the hippocampal tissue from older animals with a drug that increased histone acetylation, they were able to restore BDNF production and synaptic plasticity to levels found in younger animals.

"These findings shed light on why synapses become less efficient and more vulnerable to impairment during aging," said Xie, who led the study. "Such knowledge could help develop new drugs for cognitive aging and aging-related neurodegenerative diseases, such as Alzheimer's disease," she added.

The researchers also found that treating the hippocampal tissue from older animals with a different drug that activates a BDNF receptor also reversed the synaptic plasticity deficit in the older rats. Because histone acetylation is important in many functions throughout the body, these findings offer a potential pathway to treat aging-related synaptic plasticity deficits without interfering with histone acetylation.

"It appears that lifelong shifts in gene regulation steadily deprive the brain of a key growth factor and cause a collapse of the 'machinery' supporting memory, cognition, and the viability of neurons," said Gary Lynch, PhD, a synaptic plasticity expert at the University of California, Irvine. "The very good news suggested by this study is that it may be possible to reverse these effects."

*The research was supported by the National Institute on Aging and UCLA Older Americans Independence Center.*

[http://www.eurekalert.org/pub\\_releases/2011-12/aeco-ndw120711.php](http://www.eurekalert.org/pub_releases/2011-12/aeco-ndw120711.php)

### **Novel drug wipes out deadliest malaria parasite through starvation**

#### ***An antimalarial agent proved effective at clearing infections caused by the malaria parasite most lethal to humans – by literally starving the parasites to death***

BRONX, NY - An antimalarial agent developed by researchers at Albert Einstein College of Medicine of Yeshiva University proved effective at clearing infections caused by the malaria parasite most lethal to humans – by literally starving the parasites to death. The novel research, carried out on a small number of non-human primates, could bolster efforts to develop more potent therapies against one of the world's leading killers. The study, published in the November 11, 2011 issue of PLoS ONE, was led by senior author Vern Schramm, Ph.D., professor and Ruth Merns Chair in Biochemistry at Einstein.

Malaria is a mosquito-borne disease caused by single-celled parasites belonging to the Plasmodium genus. The U.S. Centers for Disease Control and Prevention estimated that in 2008 (the latest year for which figures are available) between 190 million and 311 million cases of malaria occurred worldwide and between 708,000 and 1.003 million people died, most of them young children in sub-Saharan Africa. Plasmodium falciparum, the malaria species most likely to cause severe infections and death, is very common in many countries in Africa south of the Sahara desert.

The Einstein researchers exploited what is arguably P. falciparum's Achilles' heel: it can't synthesize purines, vital building blocks for making DNA. Instead, the parasite must make purines indirectly, by using an enzyme called purine nucleoside phosphorylase (PNP) to make a purine precursor called hypoxanthine. By inhibiting PNP, the drug BCX4945 kills the parasites by starving them of the purines they need to survive.

After BCX4945 showed potency against laboratory cultures of P. falciparum, owl monkeys were chosen as the non-human primate model for further testing of the drug. Three animals were infected with a strain of P. falciparum that is consistently lethal without antimalarial therapy. Orally administering BCX4945 twice a day for seven days cleared the infections from all the animals between the fourth and seventh day of treatment. The monkeys remained parasite-negative for up to nine days post-treatment. Parasitic infection eventually returned in all three monkeys after treatment ended, although a lower rate of parasitic growth was observed. No signs of toxicity were observed during the study period (30 days after the first dose).

BCX4945 belongs to a class of drugs known as transition state analogs that Dr. Schramm has been developing since 1994. Transition states form in every chemical change and whenever an enzyme does its job of converting one chemical (the substrate) into another (the product). The fleeting transition-state molecule is neither substrate nor product, but something in between—a ghostly intermediate to which the enzyme clings for just one billionth of a millionth of a second.

After figuring out the brief-lived transition-state structure for a particular enzyme, Dr. Schramm is able to design transition-state analogs to knock that enzyme out of action. The analogs closely resemble the actual transition-state structure but with one big difference: they powerfully inhibit the enzyme by binding to it and not letting go.

The transition-state analog BCX4945 was chosen for this study because of its high affinity for both P. falciparum PNP and human PNP (which the parasite obtains from the red blood cells it infects). Since PNP is abundant in mammalian red blood cells and those cells are constantly replaced, BCX4945 is toxic only to the parasite and not its mammalian hosts. (Two of Dr. Schramm's other PNP inhibitors—one for T-cell cancers, the other for gout—are being evaluated in clinical trials.)

"Inhibiting PNP differs from all other current approaches for treating malaria," said Dr. Schramm. "For that reason, BCX4945 fits well with the current World Health Organization protocols for malaria treatment, which call for using combination-therapy approaches against the disease."

*The paper is titled "Plasmodium falciparum Parasites Are Killed by a Transition State Analogue of Purine Nucleoside Phosphorylase in a Primate Animal Model." Other Einstein researchers involved in the study were Steven Almo, Ph.D., lead author Maria Cassera, Ph.D. (now at Virginia Polytechnic Institute and State University), Keith Hazleton, M.D./Ph.D. candidate, Emilio Merino (now at Virginia Polytechnic Institute and State University), Meng-Chiao Ho, Ph.D., (now at Academia Sinica), Andrew Murkin, Ph.D., (now at SUNY Buffalo), and Jemy Gutierrez, Ph.D., (now at Pfizer). This research was supported primarily by the National Institute of Allergy and Infectious Disease, part of the National Institutes of Health, and early aspects of the study were funded by Medicines for Malaria.*

**Mayo Clinic collaboration finds multiple sclerosis often starts in brain's outer layers**  
***Multiple sclerosis (MS) may progress from the outermost layers of the brain to its deep parts, and isn't always an "inside-out" process as previously thought***

ROCHESTER, Minn. - Multiple sclerosis (MS) may progress from the outermost layers of the brain to its deep parts, and isn't always an "inside-out" process as previously thought, reported a new collaborative study from researchers at the Mayo Clinic and the Cleveland Clinic. The traditional understanding is that the disease begins in the white matter that forms the bulk of the brain's inside, and extends to involve the brain's superficial layers, the cortex. Study findings support an opposite, outside-in process: from the cerebrospinal fluid-filled subarachnoid space, that cushions the outside of the brain and the cortex, into the white matter. The new findings will guide researchers as they seek to further understand and treat the disease. The study was published in the December issue of the New England Journal of Medicine.

Researchers do not know precisely what causes MS, but it is thought to be an autoimmune disease in which the body's immune system attacks and destroys its own myelin. This fatty substance surrounds and protects axons, nerve cell projections that carry information, and its damage slows down or blocks messages between the brain and body, leading to MS symptoms, which can include blindness, numbness, paralysis, and thinking and memory problems.

"Our study shows the cortex is involved early in MS and may even be the initial target of disease," says Claudia F. Lucchinetti, M.D., co-lead author of the study and Mayo Clinic neurologist. "Inflammation in the cortex must be considered when investigating the causes and progression of MS", she says.

Study authors say current therapeutic options may not even address issues associated with the cortex. Understanding how the cortex is involved, therefore, is critical to creating new therapies for MS. "Measures of cortical damage will enhance enormously the power of clinical trials to determine if new medications address tissue changes of MS in all regions of the brain," says co-lead author Richard Ransohoff, M.D., a Cleveland Clinic neurologist. These measures are important because disease accumulates in the cortex over time, and inflammation in the cortex is a sign the disease has progressed.

The research is distinct because it studied brain tissues from patients in the earliest stages of MS. "What's unique about the study is, and the reason the National MS Society funded this international team of researchers, is that it offers a rare view of MS early in the disease," says Timothy Coetzee, Ph.D., Chief Research Officer at the National Multiple Sclerosis Society. "Collaborative studies like this, that deepen our understanding of the sequence of nervous system-damaging events, should offer new opportunities for stopping MS disease progression and improving quality of life for people with MS." The findings support the understanding that MS is primarily a disease of inflammation, not neurodegeneration, as some studies have recently suggested. Co-lead authors Drs. Lucchinetti and Ransohoff conclude that it is "overwhelmingly likely" that MS is fundamentally an inflammatory disease, and not a neurodegenerative Alzheimer-like disease.

**How They Did It**

The research did not at first focus on the 'outside-in' question, says Dr. Lucchinetti. Instead, the team initially wondered what tissue changes in the cortex of MS patients gave rise to indicators of cortical damage. For the last several years, researchers knew from MRI studies that the cortex was damaged very early after onset of MS, and they knew from autopsy studies that the cortex was demyelinated, as was white matter. What researchers were unable to determine, until completion of the present study, was whether findings at autopsy (usually after 30-50 years of disease) accurately reflected the indicators of cortical damage from MRI images taken after only a few months of disease. In autopsy MS tissues, cortical lesions show demyelination, but without inflammation-raising the possibility that MS cortex degenerates due to intrinsic tissue defects. Such a process would not be treatable by current MS therapies and could not be explained by present concepts of the causes of MS.

Drs. Lucchinetti and Ransohoff determined to see if early-MS cortical lesions were, or were not, inflammatory. To do so, they studied the Mayo resource of white-matter biopsies taken largely from patients with suspected tumors, but eventually proving to have MS. About one-fourth of the biopsies also included tiny fragments of cortex, which formed the focus of study. The primary question was quickly answered: cortical demyelinating lesions of early-MS patients resembled those found at autopsy in every way but one -- the early lesions were highly inflammatory. These findings were reassuring because they indicated that treatments targeting inflammation in the disease may ameliorate MS effects on both the cortex as well as the white matter.

While investigating the cortical changes in the biopsies, researchers were struck by the high frequency of cortical demyelinating lesions. Furthermore, in the white matter biopsies, which contained miniscule cortical fragments, about 20% showed inflammatory demyelination was contained entirely in the cortex.



Researchers also noted inflammation was present in the meninges, the protective membranes that cover the surface of the brain and demarcate the subarachnoid space. Meningeal inflammation and cortical demyelination were highly-associated. Looking at implications of their data, Drs. Lucchinetti and Ransohoff could weave together a proposed pathway for lesion initiation, along with known experimental data from MS animal models, and term this pathway the "outside-in" theory. The research findings also lend urgency to efforts to use MRI to "see" more deeply into the cortical lesions of MS, particularly given that cortical damage is an important correlate of progressive disability and cognitive dysfunction in MS.

*This study was funded by the National MS Society's MS Lesion Project, led by Dr. Lucchinetti, as well as the National Institutes of Health.*

*Other Mayo Clinic study authors include: Bogdan Popescu, M.D.; Reem Bunyan, M.D.; Shanu Roemer, M.D.; Joseph Parisi, M.D.; Bernd Scheithauer, M.D.; Caterina Giannini, M.D.; Stephen Weigand, M.S.; Jay Mandrekar, Ph.D.*

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[http://www.eurekalert.org/pub\\_releases/2011-12/tu-rdt120711.php](http://www.eurekalert.org/pub_releases/2011-12/tu-rdt120711.php)

## **Researchers discover that changes in bioelectric signals cause tadpoles to grow eyes in back, tail**

### ***Scientists have altered natural bioelectrical communication among cells to directly specify the type of new organ to be created at a particular location within a vertebrate organism***

MEDFORD/SOMERVILLE, Mass. - For the first time, scientists have altered natural bioelectrical communication among cells to directly specify the type of new organ to be created at a particular location within a vertebrate organism. Using genetic manipulation of membrane voltage in *Xenopus* (frog) embryos, biologists at Tufts University's School of Arts and Sciences were able to cause tadpoles to grow eyes outside of the head area.

The researchers achieved most surprising results when they manipulated membrane voltage of cells in the tadpole's back and tail, well outside of where the eyes could normally form. "The hypothesis is that for every structure in the body there is a specific membrane voltage range that drives organogenesis," said Tufts post-doctoral fellow Vaibhav P. Pai Ph.D., the first author of the paper, entitled "Transmembrane Voltage Potential Controls Embryonic Eye Patterning in *Xenopus laevis*." "These were cells in regions that were never thought to be able to form eyes. This suggests that cells from anywhere in the body can be driven to form an eye."

To do this, they changed the voltage gradient of cells in the tadpoles' back and tail to match that of normal eye cells. The eye-specific gradient drove the cells in the back and tail—which would normally develop into other organs—to develop into eyes.

These findings break new ground in the field of biomedicine because they identify an entirely new control mechanism that can be capitalized upon to induce the formation of complex organs for transplantation or regenerative medicine applications, according to Michael Levin, Ph.D., professor of biology and director of the Center for Regenerative and Developmental Biology at Tufts University's School of Arts and Sciences. Levin is senior and corresponding author on the work published in the journal *Development* online December 7 2011, in advance of print.



***Eye developed in midsection of tadpole. Michale Levin and Sherry Aw***

"These results reveal a new regulator of eye formation during development, and suggest novel approaches for the detection and repair of birth defects affecting the visual system," he said. "Aside from the regenerative medicine applications of this new technique for eyes, this is a first step to cracking the bioelectric code."

### **Signals Turn On Eye Genes**

From the outset of their research, the Tufts' biologists wanted to understand how cells use natural electrical signals to communicate in their task of creating and placing body organs. In recent research, Tufts biologist Dany S. Adams showed that bioelectrical signals are necessary for normal face formation in the *Xenopus* (frog) embryos. In the current set of experiments, the Levin lab identified and marked hyperpolarized (more negatively charged) cell clusters located in the head region of the frog embryo. They found that these cells expressed genes that are involved in building the eye called Eye Field Transcription Factors (EFTFs). Sectioning of the embryo through the developed eye and analyzing the eye regions under fluorescence microscopy showed that the hyperpolarized cells contributed to development of the lens and retina. The researchers hypothesized that these cells turned on genes that are necessary for building the eye.



## Changing the Signals Lead to Defects

Next, the researchers were able to show that changing the bioelectric code, or depolarizing these cells, affected normal eye formation. They injected the cells with mRNA encoding ion channels, which are a class of gating proteins embedded in the membranes of the cell. Like gates, each ion channel protein selectively allows a charged particle to pass in and out of the cell.

Using individual ion channels that allow, the researchers changed the membrane potential of these cells. This affected expression of EFTF genes, causing abnormalities to occur: Tadpoles from these experiments were normal except that they had deformed or no eyes at all. Further, the Tufts biologists were also able to show that they could control the incidence of abnormal eyes by manipulating the voltage gradient in the embryo. "Abnormalities were proportional to the extent of disruptive depolarization," said Pai. "We developed techniques to raise or lower voltage potential to control gene expression."

## Electric Properties of Cells Can Be Manipulated to Generate Specific Organs

The researchers achieved most surprising results when they manipulated membrane voltage of cells in the tadpole's back and tail, well outside of where the eyes could normally form.

"The hypothesis is that for every structure in the body there is a specific membrane voltage range that drives organogenesis," said Pai. "By using a specific membrane voltage, we were able to generate normal eyes in regions that were never thought to be able to form eyes. This suggests that cells from anywhere in the body can be driven to form an eye."

Levin and his colleagues are pursuing further research, additionally targeting the brain, spinal cord, and limbs. The findings, he said "will allow us to have much better control of tissue and organ pattern formation in general. We are developing new applications of molecular bioelectricity in limb regeneration, brain repair, and synthetic biology." Additional authors include post-doctoral fellow Sherry Aw, Tufts Postdoctoral Associate Tal Shomrat, and Research Associate Joan M. Lemire. Funding for this research came from the National Institutes of Health. *"Transmembrane voltage potential controls embryonic eye patterning in Xenopus laevis," Vaibhav P. Pai, Sherry Aw, Tal Shomrat, Joan M. Lemire, Development, published online before print December 20, 2011, doi:10.1242/dev.073759*

<http://www.physorg.com/news/2011-12-geminid-meteor-shower.html>

## Geminid meteor shower 2011

***Its the finale of this year's meteor showers: The Geminids will start appearing on Dec. 7 and should reach peak activity around the 13th and 14th.***

This shower could put on a display of up to 100+ meteors (shooting stars) per hour under good viewing conditions. However, conditions this year are not ideal with the presence of a waning gibbous Moon (which will be up from mid-evening until morning). But seeing meteors every few minutes is quite possible. Geminid meteors are often slow and bright with persistent colored trails which can linger for a while after the meteor has burned up.

There is something unusual about the Geminid meteor shower, as normally meteor showers are caused by the Earth ploughing through the debris streams created by comets and their tails. But the object that created the specific stream of debris associated with the Geminids is not a dusty icy comet, but a rocky asteroid called Phaethon 3200. Phaethon 3200 belongs to a group of asteroids whose orbit cross the Earth's. It turns out to be an unusual member of that group: Not only does it pass closer to the Sun than the others but it also has a different color, suggesting a different composition to most asteroids.

One of the curious things about the Geminid particles is that they are more solid than meteoroids known to come from comets. This is good for meteor watchers; giving us brighter meteors. Observations by astronomers over decades have shown that meteor rates have increased as we reach denser parts of the stream.

It is not known exactly when the asteroid was deflected into its current orbit, but if it was originally a comet it would have taken a long time for all the ices to have been lost. However it is possible that it may have been a stony asteroid with pockets of ice. We are unsure of the origins and appearance of Phaethon 3200, but its orbit has left us with a unique legacy every December, with little streaks of light known as the Geminid meteor shower.

You will only need your eyes to watch the meteor shower, you do not need telescopes binoculars etc, but you will need to be patient and comfortable. See this handy guide on how to observe meteors.

During a meteor shower, meteors originate from a point in the sky called the radiant and this gives rise to the showers name e.g. The Geminids radiant is in Gemini, Perseids radiant is in Perseus etc.

Don't be misled by thinking you have to look in a particular part of or direction of the sky, as meteors will appear anywhere and will do so at random. You will notice that if you trace back their path or trajectory it will bring you to the meteor showers radiant. The exception to this rule is when you see a sporadic or rogue meteor.

Tell your friends, tell your family and tell everyone to look up and join in with the Geminid meteorwatch on the 12th to the 14th December 2011. Use the #meteorwatch hashtag on twitter and visit [meteorwatch.org](http://meteorwatch.org) for tips and guides on how to see and enjoy the Geminids and other meteor showers. *Source: Universe Today*

<http://www.newscientist.com/article/dn21251-first-top-predator-was-giant-shrimp-with-amazing-eyes.html>

## **First top predator was giant shrimp with amazing eyes**

***Half a billion years ago, sea creatures fled from a terrifying new creature: a gigantic primordial shrimp with pin-sharp vision.***

**18:00 07 December 2011 by Michael Marshall**

It is one of the oldest known animals with compound eyes, the hallmark of modern insects and crustaceans.

Anomalocaris – the name means "strange shrimp" – is the earliest known example of a top predator. At 90 to 200 centimetres long, it was the largest animal in the Cambrian seas. It had formidable grasping claws, which allowed it to grab its prey and pull it into its mouth. Lacking legs, it must have swum in open water.

That raises a question: how did it find its prey? It had eyes, but all fossils discovered until now have been in poor condition, so we didn't know how well it could see. Now John Paterson of the University of New England in Armidale, New South Wales, Australia, and colleagues have found a pair of exceptionally well-preserved eyes, 515 million years old, on Kangaroo Island off Australia's south coast. "Anomalocaris had remarkable vision, rivalling or exceeding that of most living insects and crustaceans," Paterson says.

### **All-seeing eye**

The eyes were on stalks on the strange shrimp's head, and each was 2 to 3 centimetres across – about the size of an olive. They were covered with lenses, each 70 to 110 micrometres in diameter. That means each eye had at least 16,000 lenses. "Very few modern animals, particularly arthropods, have eyes as sophisticated as this," says Paterson. Houseflies, for instance, have a mere 3000 lenses. The only comparable species are some predatory dragonflies that have up to 28,000 lenses in each eye. Anomalocaris's acute eyesight probably allowed it to seek out its prey in the brightly lit upper layers of the ocean.



*Eyes of a killer* (Image: Katrina Kenny/University of Adelaide)

The first arthropods – the group that includes insects, spiders and Anomalocaris – probably had compound eyes, says Graham Budd of Uppsala University in Sweden. "The arthropods have diversified spectacularly, but these inventions from the Cambrian have been retained all the way through."

To make use of its eyes, Anomalocaris must have had a reasonable brain, Budd says. Indeed, molecular evidence suggests that key structures from the human brain date back to the first complex animals, alive at least 600 million years ago – long before Anomalocaris.

### **Feeding time**

It's not clear what Anomalocaris ate. Paterson points to bite marks and other injuries found on trilobites from the period, which may indicate Anomalocaris targeted them. But there are suggestions that its mouth was too weak to break their shells, in which case it may have had to make do with soft-bodied animals.

Paterson says the threat of Anomalocaris would have forced other species, both prey and other predators, to evolve rapidly. Hard shells were an obvious way to go, and evolved soon after. Anomalocaris itself was not well armoured: it probably had a soft exoskeleton made of chitin, rather like a prawn.

Nevertheless it was successful. Animals like Anomalocaris survived until 480 million years ago.

*Journal reference: Nature, DOI: 10.1038/nature10689*

[http://www.eurekalert.org/pub\\_releases/2011-12/aafc-ild120111.php](http://www.eurekalert.org/pub_releases/2011-12/aafc-ild120111.php)

## **Intermittent, low-carbohydrate diets more successful than standard dieting** ***Present possible intervention for breast cancer prevention***

SAN ANTONIO - An intermittent, low-carbohydrate diet was superior to a standard, daily calorie-restricted diet for reducing weight and lowering blood levels of insulin, a cancer-promoting hormone, according to recent findings. Researchers at Genesis Prevention Center at University Hospital in South Manchester, England, found that restricting carbohydrates two days per week may be a better dietary approach than a standard, daily calorie-restricted diet for preventing breast cancer and other diseases, but they said further study is needed.

"Weight loss and reduced insulin levels are required for breast cancer prevention, but [these levels] are difficult to achieve and maintain with conventional dietary approaches," said Michelle Harvie, Ph.D., SRD, a

research dietician at the Genesis Prevention Center, who presented the findings at the 2011 CTRC-AACR San Antonio Breast Cancer Symposium, held Dec. 6-10, 2011.

Harvie and her colleagues compared three diets during four months for effects on weight loss and blood markers of breast cancer risk among 115 women with a family history of breast cancer. They randomly assigned patients to one of the following diets: a calorie-restricted, low-carbohydrate diet for two days per week; an "ad lib" low-carbohydrate diet in which patients were permitted to eat unlimited protein and healthy fats, such as lean meats, olives and nuts, also for two days per week; and a standard, calorie-restricted daily Mediterranean diet for seven days per week.

Data revealed that both intermittent, low-carbohydrate diets were superior to the standard, daily Mediterranean diet in reducing weight, body fat and insulin resistance. Mean reduction in weight and body fat was roughly 4 kilograms (about 9 pounds) with the intermittent approaches compared with 2.4 kilograms (about 5 pounds) with the standard dietary approach. Insulin resistance reduced by 22 percent with the restricted low-carbohydrate diet and by 14 percent with the "ad lib" low-carbohydrate diet compared with 4 percent with the standard Mediterranean diet.

"It is interesting that the diet that only restricts carbohydrates but allows protein and fats is as effective as the calorie-restricted, low-carbohydrate diet," Harvie said. She and her colleagues plan to further study carbohydrate intake and breast cancer.

*This study was funded by the Genesis Breast Cancer Prevention Appeal ([www.genesisuk.org](http://www.genesisuk.org)).*

[http://www.eurekalert.org/pub\\_releases/2011-12/uotw-efe120211.php](http://www.eurekalert.org/pub_releases/2011-12/uotw-efe120211.php)

## **Evidence for early 'bedding' and the use of medicinal plants at a South African rock shelter**

### ***An international team of archaeologists is reporting 77,000-year-old evidence for preserved plant bedding and the use of insect-repelling plants in a rock shelter in South Africa***

An international team of archaeologists is reporting 77,000-year-old evidence for preserved plant bedding and the use of insect-repelling plants in a rock shelter in South Africa. This discovery is 50,000 years older than earlier reports of preserved bedding and provides a fascinating insight into the behavioural practices of early modern humans in southern Africa.

The team, led by Professor Lyn Wadley of the University of the Witwatersrand, Johannesburg, in collaboration with Christopher Miller (University of Tübingen, Germany), Christine Sievers and Marion Bamford (University of the Witwatersrand), and Paul Goldberg and Francesco Berna (Boston University, USA), is reporting the discovery in the scientific journal *Science*, to be published on Friday, 9 December 2011.

The ancient bedding was uncovered during excavations at Sibudu rock shelter (KwaZulu-Natal province, South Africa), where Lyn Wadley, honorary professor at the University of the Witwatersrand, has been digging since 1998. At least 15 different layers at the site contain plant bedding, dated between 77,000 and 38,000 years ago. The bedding consists of centimetre-thick layers of compacted stems and leaves of sedges and rushes, extending over at least one square metre and up to three square metres of the excavated area. Christine Sievers, of the University of the Witwatersrand, was able to identify nutlets from several types of sedges and rushes used in the construction of the bedding.

The oldest evidence for bedding at the site is particularly well-preserved, and consists of a layer of fossilised sedge stems and leaves, overlain by a tissue-paper-thin layer of leaves, identified by botanist Marion Bamford as belonging to *Cryptocarya woodii*, or River Wild-quince. The leaves of this tree contain chemicals that are insecticidal, and would be suitable for repelling mosquitoes.

"The selection of these leaves for the construction of bedding suggests that the early inhabitants of Sibudu had an intimate knowledge of the plants surrounding the shelter, and were aware of their medicinal uses. Herbal medicines would have provided advantages for human health, and the use of insect-repelling plants adds a new dimension to our understanding of behaviour 77,000 years ago," says Professor Lyn Wadley.

"The inhabitants would have collected the sedges and rushes from along the uThongathi River, located directly below the site, and laid the plants on the floor of the shelter. The bedding was not just used for sleeping, but would have provided a comfortable surface for living and working," adds Wadley.

Microscopic analysis of the bedding, conducted by Christopher Miller, junior-professor for geoarchaeology at the University of Tübingen, suggests that the inhabitants repeatedly refurbished the bedding during the course of occupation. The microscopic analysis also demonstrated that after 73,000 years ago, the inhabitants of Sibudu regularly burned the bedding after use.

"They lit the used bedding on fire, possibly as a way to remove pests. This would have prepared the site for future occupation and represents a novel use of fire for the maintenance of an occupation site," says Miller.

The preserved bedding is also associated with the remains of numerous fireplaces and ash dumps. Beginning at 58,000 years ago, the number of hearths, bedding and ash dumps increases dramatically. The archaeologists believe that this is a result of intensified occupation of the site. In the article, the archaeologists argue that the increased occupation may correspond with changing demographics within Africa at the time. By around 50,000 years ago, modern humans began expanding out of Africa, eventually replacing archaic forms of humans in Eurasia, including the Neanderthals.

This discovery adds to a long list of important finds at Sibudu over the past decade, including perforated seashells, believed to have been used as beads, and sharpened bone points, likely used for hunting.

Wadley and others have also presented early evidence from the site for the development of bow and arrow technology, the use of snares and traps for hunting, and the production of glue for hafting stone tools.

[http://www.eurekalert.org/pub\\_releases/2011-12/uomr-rss120711.php](http://www.eurekalert.org/pub_releases/2011-12/uomr-rss120711.php)

### **Research study shows link between earthquakes and tropical cyclones** ***New study may help scientists identify regions at high risk for earthquakes***

SAN FRANCISCO – A groundbreaking study led by University of Miami (UM) scientist Shimon Wdowinski shows that earthquakes, including the recent 2010 temblors in Haiti and Taiwan, may be triggered by tropical cyclones (hurricanes and typhoons). Wdowinski will discuss his findings during a presentation at the 2011 AGU Fall Meeting in San Francisco.

"Very wet rain events are the trigger," said Wdowinski, associate research professor of marine geology and geophysics at the UM Rosenstiel School of Marine and Atmospheric Science. "The heavy rain induces thousands of landslides and severe erosion, which removes ground material from the Earth's surface, releasing the stress load and encouraging movement along faults."

Wdowinski and a colleague from Florida International University analyzed data from quakes magnitude-6 and above in Taiwan and Haiti and found a strong temporal relationship between the two natural hazards, where large earthquakes occurred within four years after a very wet tropical cyclone season.

During the last 50 years three very wet tropical cyclone events – Typhoons Morakot, Herb and Flossie – were followed within four years by major earthquakes in Taiwan's mountainous regions. The 2009 Morakot typhoon was followed by a M-6.2 in 2009 and M-6.4 in 2010. The 1996 Typhoon Herb was followed by M-6.2 in 1998 and M-7.6 in 1999 and the 1969 Typhoon Flossie was followed by a M-6.2 in 1972. The 2010 M-7 earthquake in Haiti occurred in the mountainous region one-and-a-half years after two hurricanes and two tropical storms drenched the island nation within 25 days.

The researchers suggest that rain-induced landslides and excess rain carries eroded material downstream. As a result the surface load above the fault is lessened. "The reduced load unclamp the faults, which can promote an earthquake," said Wdowinski. Fractures in Earth's bedrock from the movement of tectonic plates, known as faults, build up stress as they attempt to slide past each other, periodically releasing the stress in the form of an earthquake.

According to the scientists, this earthquake-triggering mechanism is only viable on inclined faults, where the rupture by these faults has a significant vertical movement. Wdowinski also shows a trend in the tropical cyclone-earthquake pattern exists in M-5 and above earthquakes. The researchers plan to analyze patterns in other seismically active mountainous regions – such as the Philippines and Japan – that are subjected to tropical cyclones activity.

<http://www.physorg.com/news/2011-12-wine-dregs-shown-cows.html>

### **Wine dregs shown to improve cows' milk** ***Feeding dairy cows the stems, seeds and skins from wine grapes boosts milk production, research shows***

Feeding dairy cows the stems, seeds and skins from wine grapes boosts milk production and dramatically cuts the animal's methane emissions, Australian researched published Thursday shows.

Scientists found that supplementing the cows' feed with grape marc - the leftover material from wine-making - reduced cow emissions by 20 percent and increased milk production by five percent. It also led to more healthy fatty acids in their milk, the research by Victoria's Department of Primary Industries found.

Scientist Peter Moate said researchers were stunned by the results, with the cut to methane emissions thought to represent the largest reduction of its kind ever attained through the use of a feed supplement. "We've managed to utilise what is currently a waste product for the wine industry and turn it into a very valuable feed source," Moate said.

The scientists supplemented the diet of dairy cows with five kilograms of dried grape marc over 37 days and compared the results with other animals fed conventional fodder.



Moate said the research showed that fatty acids in the grape marc milk were six times higher than with standard autumn feed. "These particular fatty acids are extremely potent in their ability to benefit heart health and are also known to help fight cancer, diabetes and arthritis," he said. Moate added there were also indications that cows fed grape marc produced milk with higher levels of healthy anti-oxidants and further tests were being conducted to verify this.

The research is part of a wider programme looking at the use of feed supplements to reduce methane emissions, including brewers' grains and cold-pressed canola meal. The dairy industry in Victoria state provides than 85 percent of Australia's dairy exports, producing 5.9 billion litres of raw milk each year from a herd of around one million cows. (c) 2011 AFP

<http://www.bbc.co.uk/news/health-16086004>

### **Rare gene links vitamin D and multiple sclerosis**

***A rare genetic variant which causes reduced levels of vitamin D appears to be directly linked to multiple sclerosis, says an Oxford University study.***

UK and Canadian scientists identified the mutated gene in 35 parents of a child with MS and, in each case, the child inherited it. Researchers say this adds weight to suggestions of a link between vitamin D deficiency and MS. The study is in *Annals of Neurology*.

Multiple sclerosis is an inflammatory disease of the central nervous system (the brain and spinal cord).

Although the cause of MS is not yet conclusively known, both genetic and environmental factors and their interactions are known to be important.

Oxford University researchers, along with Canadian colleagues at the University of Ottawa, University of British Columbia and McGill University, set out to look for rare genetic changes that could explain strong clustering of MS cases in some families in an existing Canadian study. They sequenced all the gene-coding regions in the genomes of 43 individuals selected from families with four or more members with MS.

The team compared the DNA changes they found against existing databases, and identified a change in the gene CYP27B1 as being important. When people inherit two copies of this gene they develop a genetic form of rickets - a disease caused by vitamin D deficiency. Just one copy of the mutated CYP27B1 gene affects a key enzyme which leads people with it to have lower levels of vitamin D.

#### **Overwhelming odds**

The researchers then looked for the rare gene variant in over 3,000 families of unaffected parents with a child with MS. They found 35 parents who carried one copy of this variant along with one normal copy.

In every one of these 35 cases, the child with MS had inherited the mutated version of the gene. The likelihood of this gene's transmission being unconnected to the MS is billions to one against, say the researchers.

Prof George Ebers, lead study author at Oxford University, says the odds are overwhelming. "All 35 children inheriting the variant is like flipping a coin 35 times and getting 35 heads, entailing odds of 32 billion to one against." He added: "This type of finding has not been seen in any complex disease. The uniform transmission of a variant to offspring with MS is without precedent but there will have been interaction with other factors."

Prof Ebers believes that this new evidence adds to previous observational studies which have suggested that sunshine levels around the globe - the body needs sunshine to generate vitamin D - are linked to MS.

He maintained that there was now enough evidence to carry out large-scale studies of vitamin D supplements for preventing multiple sclerosis.

"It would be important particularly in countries like Scotland and the rest of the UK where sunshine levels are low for large parts of the year. Scotland has the greatest incidence of multiple sclerosis of any country in the world."

Dr Doug Brown, head of biomedical research at the MS Society, called it an important development.

"This shines more light on the potential role of vitamin D deficiency on increasing the risk of developing MS.

"This research is gathering momentum and will be the subject of discussion at an international expert meeting in the USA this month, the outcomes of which will shape future research that will give us the answers we so desperately need about the potential risks and benefit of vitamin D supplementation."

Paul Comer, from the charity MS Trust, said the research strengthened the case for vitamin D being one potential contributory cause of MS.

"Current opinion suggests that a combination of genetic predisposition, environmental factors such as exposure to sunlight and possibly some sort of trigger, such as a viral infection, interact in some way to start the development of MS.

"We welcome any research that clarifies the interplay between these factors. This is another step towards finding ways to reduce the risk of developing MS, but it is likely to be some years yet before we can gauge the significance of vitamin D deficiency to MS."

[http://www.eurekalert.org/pub\\_releases/2011-12/rpi-rda120911.php](http://www.eurekalert.org/pub_releases/2011-12/rpi-rda120911.php)

### **Researchers design Alzheimer's antibodies A surprisingly simple method to target harmful proteins**

Troy, N.Y. – Researchers at Rensselaer Polytechnic Institute have developed a new method to design antibodies aimed at combating disease. The surprisingly simple process was used to make antibodies that neutralize the harmful protein particles that lead to Alzheimer's disease. The process is reported in the Dec. 5 Early Edition of the journal Proceedings of the National Academy of Sciences (PNAS). The process, outlined in the paper, titled "Structure-based design of conformation- and sequence-specific antibodies against amyloid  $\beta$ ," could be used as a tool to understand complex disease pathology and develop new antibody-based drugs in the future.

Antibodies are large proteins produced by the immune system to combat infection and disease. They are comprised of a large Y-shaped protein topped with small peptide loops. These loops bind to harmful invaders in the body, such as a viruses or bacteria. Once an antibody is bound to its target, the immune system sends cells to destroy the invader. Finding the right antibody can determine the difference between death and recovery.

Scientists have long sought methods for designing antibodies to combat specific ailments. However, the incredible complexity of designing antibodies that only attached to a target molecule of interest has prevented scientists from realizing this ambitious goal. When trying to design an antibody, the arrangement and sequence of the antibody loops is of utmost importance. Only a very specific combination of antibody loops will bind to and neutralize each target. And with billions of different possible loop arrangements and sequences, it is seemingly impossible to predict which antibody loops will bind to a specific target molecule.

The new antibody design process was used to create antibodies that target a devastating molecule in the body: the Alzheimer's protein. The research, which was led by Assistant Professor of Chemical and Biological Engineering Peter Tessier, uses the same molecular interactions that cause the Alzheimer's proteins to stick together and form the toxic particles that are a hallmark of the disease.

"We are actually exploiting the same protein interactions that cause the disease in the brain to mediate binding of antibodies to toxic Alzheimer's protein particles," Tessier said.

Alzheimer's disease is due to a specific protein – the Alzheimer's protein – sticking together to form protein particles. These particles then damage the normal, healthy functions of the brain. The formation of similar toxic protein particles is central to diseases such as Parkinson's and mad cow disease.

Importantly, the new Alzheimer's antibodies developed by Tessier and his colleagues only latched on to the harmful clumped proteins and not the harmless monomers or single peptides that are not associated with disease.

Tessier and his colleagues see the potential for their technique being used to target and better understand similar types of protein particles in disorders such as Parkinson's disease. "By binding to specific portions of the toxic protein, we could test hypotheses about how to prevent or reverse cellular toxicity linked to Alzheimer's disease," Tessier said. In the long term, as scientists learn more about methods to deliver drugs into the extremely well-protected brain tissue, the new antibody research may also help to develop new drugs to combat disorders such as Alzheimer's disease.

*The research was funded by the Alzheimer's Association, the National Science Foundation (NSF), and the Pew Charitable Trust. Tessier was joined in the research by Rensselaer graduate students Joseph Perchiaica (co-first author), Ali Reza Ladiwala (co-first author), and Moumita Bhattacharya.*

<http://www.physorg.com/news/2011-12-music-expert-christmas-limited-season.html>

### **Music expert says Christmas music not just limited to the season, and happiness it brings may be the reason**

***If it seems the sounds of the season are being heard more and more out of season, a Kansas music expert says there's a reason.***

PhysOrg.com - If it seems the sounds of the season -- "Jingle Bells," "Deck the Halls," "Joy to the World" and other holiday favorites -- are being heard more and more out of season, a Kansas State University music expert says there's a reason.

Hearing Christmas music before December is becoming more common, and Jana Fallin, professor of music education at Kansas State, says there may be a deeper meaning behind this trend.

"As far as people's obsession with Christmas music, I think they just like that warm, happy, joyous feeling it brings," Fallin said. "Part of it is what we want the music to represent, because we want Christmas to be about family, full of love and all of those thoughts. I think people just want to be happy."

Fallin said the meaning found in Christmas music is linked to the brain's limbic system, which contains the amygdala, the location of emotional responses, and the hippocampus, the area that consolidates memory.

"You know how you hear a song and you remember the person you were dancing with at the senior prom? It moves you around in time through those memories and emotions in the brain," she said. "All of that is going on with Christmas carols because it takes us back to our childhood. When we hear them, we remember gifts that we received as children or family members that are no longer with us."

In the 15th century, priests used Christmas carols to tell the story of the birth of Jesus because of the high levels of illiteracy at the time. Fallin said carols were simple and easy to sing, which helped people remember the aspects of the story.

Christmas music has since evolved into a holiday tradition. Fallin says the custom of carols consists of four categories: religious, secular, traditional and humorous. Religious tunes relay the story of Jesus' birth; secular music involves tales of Santa Claus and Christmas love stories; traditional songs include holiday classics such as "We Wish You a Merry Christmas"; and the humorous genre is represented in such songs as "Grandma Got Run Over by a Reindeer."

This tradition of holiday music creates a sense of timelessness surrounding certain carols, but it can also make it difficult for artists to write new Christmas music, Fallin said. "I think it is harder for more contemporary artists to get original Christmas songs to become a hit," she said. "Some of them are just so trite, so sometimes I don't like the new stuff, and sometimes I do. It's just kind of whatever speaks to you."

Fallin suggests people look up their favorite artist online if they are looking for Christmas music that differs from the mainstream. The singer or songwriter may have recorded several original songs in the holiday genre or created a unique version of a classic carol that may be enjoyable.

While Christmas music may be an obsession for some, or a tolerated tradition for others, Fallin says it's hard to deny that carols are a major component of the holiday season. "All celebrations have music -- weddings, funerals, graduations -- and we know through research that there has never been a culture that didn't have music, even early on," Fallin said. "So music helps us celebrate the traditions of our culture, and certainly Christmas music does that. It helps us celebrate."

*Provided by Kansas State University*

<http://medicalxpress.com/news/2011-12-perils-drunken.html>

### **The perils of drunken walking**

#### ***Drinking and driving is a much-publicized, dangerous combination, but is walking after drinking any safer?***

Medical Xpress - "No, alcohol impairs your physical ability, period," said trauma surgeon Dr. Thomas Esposito at Loyola University Health System in Maywood, Ill. Every movement ranging from driving a car to simply walking to the bathroom is compromised," Esposito said. "Alcohol impairs your judgment, reflexes and coordination. Alcohol is nothing more than a socially acceptable, over-the-counter stimulant/depressant and, especially during the holidays, alcohol is frequently abused."

A trauma surgeon for more than 25 years, Esposito has witnessed the tragic aftermath of drunken walking in his own work many times. "From July 2009 to June 2010, 105 people were treated at Loyola after being struck by cars. Fifty-five had their blood-alcohol content checked. Of those, 16 individuals, or 29 percent, were found to have had some level of alcohol in their system," said Esposito, who is chief of the division of trauma, surgical critical care and burns in the Department of Surgery, Loyola University Chicago Stritch School of Medicine. "Thirteen individuals, or 24 percent, had blood-alcohol concentrations at or above .08 percent, the accepted level for intoxication."

In 2005, the journal Injury Prevention reported that New Year's Day is more deadly for pedestrians than any other day of the year. From 1986 to 2002, 410 pedestrians were killed on New Year's Day. Fifty-eight percent of those killed had high blood-alcohol concentrations (BAC).

Alcohol also plays a significant role in the deaths of pedestrians throughout the year, according to the Insurance Institute for Highway Safety. In 2008, 38 percent of fatally injured pedestrians 16 and older had blood-alcohol concentrations at or above 0.08 percent, which is the legal definition for impaired driving in Illinois. The percentage rose to 53 percent for deaths occurring between 9 p.m. and 6 a.m. Fourteen percent of pedestrian deaths involved drivers with blood-alcohol content at or above .08 percent.

"If they had been driving and were stopped by police, they would have been arrested for driving under the influence," Esposito said.

He added that those statistics don't take into account the people who suffer injuries in their homes from unintentional causes and violence after drinking.

"It's not just walking outside. We often see people who have been drinking that have fallen down the stairs or tripped at home and injured themselves. Others have unwisely chosen to 'get into it' with guns, knives, bottles and fists," Esposito said.

Loyola University Health System's hospital is the only Level 1 Trauma Center in Illinois – and one of a select group nationwide – to be verified by the American College of Surgeons. A complete array of medical, surgical and ancillary services is available through an interdisciplinary program that serves the total needs of injured adult or pediatric patients from prevention through rehabilitation, 24 hours a day. These services include hospital transport, emergency medicine, general surgery and its subspecialties - such as orthopaedics, neurosurgery and others - critical care, nursing and a multitude of others including social work, rehabilitation and nutrition.

The Burn & Shock Trauma Institute serves as the research arm of Loyola's Burn and Trauma Centers investigating problems in post-injury immunosuppression, wound healing and nutritional support. The multidisciplinary institute also supports an injury prevention program, which conducts community outreach activities. If you drink and plan to walk on New Year's Eve, or any other day of the year, you have to take special care, Esposito said. **Some tips:**

***Like Rudolph, be a beacon of light. "If planning on walking at night, don't wear dark clothing that can make it difficult for drivers to see you."***

***Stay out of the road. "Walk solely on the sidewalks and cross at designated crosswalks."***

***Enforce the buddy system. "It's a good idea to walk in a group, which is easier for drivers to spot, and try to walk with at least one person who has not been drinking, a designated chaperone or escort."***

***Give pedestrians a brake. "Drivers need to take extra care when in restaurant or bar districts, since intoxicated pedestrians have slower reflexes and can be unpredictable."***

***Be a good host. "People hosting parties in which alcohol is consumed have as much of an obligation to watch over their guests who are walking home as they do with those who may be driving."***

#### **Grab a Pillow, Not a Cab**

"You have to be able to assess someone's perceived ability to safely get from one place to the other," Esposito said. "If their mode of transportation is a car, you do things to prevent them from driving, such as calling them a cab or finding them an unimpaired chauffeur. If that mode of transportation is their legs, then you either drive them – assuming you're not impaired – or make them stay at home with you."

Even if a guest stays at your home, you should be aware that they could trip and fall down the stairs, Esposito said. "So you don't want to send them up to the second-story bedroom or down to the basement sofa."  
*Provided by Loyola University Health System*

<http://medicalxpress.com/news/2011-12-alzheimer-vaccine-memory-mice.html>

#### **Alzheimer's vaccine cures memory of mice**

***A vaccine that slows the progression of Alzheimer's disease and other types of dementia has been developed by researchers at the University of Sydney's Brain and Mind Research Institute (BMRI).***

Medical Xpress - The vaccine, which targets a protein known as tau, prevents the ongoing formation of neurofibrillary tangles in the brain of a mouse with Alzheimer's disease. This progressive neurodegenerative disease affects more than 35 million people worldwide. The tau protein is also involved in front temporal dementia, the second most common form of dementia in people younger than 65 years. The results of the study which led to the production of the vaccine have been published today in the scientific journal PLoS ONE.

Lead author on the study, Associate Professor Lars Ittner, from the Alzheimer's and Parkinson's Disease Laboratory says: "Our study is the first to show that a vaccine targeting the tau protein can be effective once the disease has already set in. "The vaccine appears to have a preventative effect: slowing the development of further tangles, rather than clearing existing ones, but the exact mechanism involved is not yet understood," he said.

According to Associate Professor Ittner, scientists have been working on vaccines targeting the amyloid plaques seen in Alzheimer's for many years with a few currently in clinical trials. "Most of the other vaccines targeting tau were tested only before or around the onset of the disease in animal models, but the vast majority of people with Alzheimer's disease are only diagnosed after the symptoms have appeared. "We are already collaborating with the US pharmaceutical industry to develop this new vaccine for humans.

"Although we have a long way to go before the vaccine might be available for human use, these early results are very promising and a great reward for the countless hours spent in the lab by me and my team!"

*Provided by University of Sydney*



<http://www.scientificamerican.com/article.cfm?id=contagion-controversy-erupts>

**Contagion: Controversy Erupts over Man-Made Pandemic Avian Flu Virus**  
***Two teams of scientists have independently constructed a deadly strain of flu. Some say the results should never be published***

**By Jeneen Interlandi | Friday, December 9, 2011 | 22**

It's a rare kind of research that incites a frenzied panic before it's even published. But it's flu season, and influenza science has a way of causing a stir this time of year.

Epidemiologists have long debated the pandemic potential of H5N1, a.k.a. avian bird flu. On one hand, the virus spreads too inefficiently between humans to seem like much of a threat: it has caused less than 600 known cases of human flu since first emerging in 1997. On the other hand, when it does spread, it can be pretty deadly: nearly 60 percent of infected humans died from the virus. For years now, the research has suggested that any mutations that enhanced the virus's ability to spread among humans, would simultaneously make it less deadly. But in a recent batch of as-yet-unpublished studies, two scientists - Yoshihiro Kawaoka from the University of Wisconsin, Madison and Ron Fouchier of Erasmus Medical Center, in the Netherlands - have shown otherwise.

Working separately, they each hit on a combination of mutations (five, in Dr. Fouchier's case) that makes H5N1 airborne (enabling it to spread readily between humans), without making it less deadly. In laboratory experiments, ferrets infected with this mutant strain passed it to other ferrets in nearby cages (ferrets are a common subject of flu studies because they react to flu viruses in a similar way to humans). A significant proportion of infected subjects died.

Efforts to publish those findings have been fraught. Critics say that making the methodology or gene sequences widely available, amounts to giving would-be bioterrorists an easy recipe. They also worry that these manmade strains might escape from the lab.

Proponents counter that the threat of a global pandemic, were this mutated strain to arise in nature, is far greater than the threat of bioterrorism. Understanding what combination of mutations could transform H5N1 into a human pandemic virus, helps epidemiologists know what to watch out for in the wild, and gives them a leg up on preparing countermeasures; they can, for example, test existing H5N1 vaccines and antiviral drugs against the new strain in the lab, before it actually emerges in the natural world.

Both papers are being reviewed by the National Science Advisory Board for Biosecurity (NSABB), which will then advise researchers and journal editors how to proceed. In the meantime, most experts agree that we need a better way.

"This is not new for science," says Michael Osterholm, director of the Center for Infectious Disease Research and Policy at the University of Minnesota, Twin Cities and a member of the NSABB. "Physicists have been doing sensitive, classified, and need-to-know work for 70 years, including academic researchers. We have to find a way to do the same in the health sciences, to work on agents that yield important information without compromising our safety and security."

<http://medicalxpress.com/news/2011-12-tropical-disease-experts-opportunity-global.html>

**Tropical disease experts report missed opportunity to transform global HIV/AIDS fight**  
***Global HIV/AIDS prevention and treatment efforts are missing a major opportunity to significantly improve health conditions in poor countries by simply adding low-cost care for the many other chronic and disabling diseases***

Global HIV/AIDS prevention and treatment efforts are missing a major opportunity to significantly improve health conditions in poor countries by simply adding low-cost care for the many other chronic and disabling diseases routinely afflicting and often killing these same patients, according to a panel of disease experts who spoke at the annual meeting of the American Society of Tropical Medicine and Hygiene (ASTMH).

"People want better health; they do not understand why we silo diseases," said Judd Walson, a global health and infectious disease expert at the University of Washington. "If you die from malaria, you don't care that your HIV was treated. Communities want us to leverage the resources we have to treat and prevent disease as effectively as possible."

Walson and his colleagues on the panel noted that many victims of HIV/AIDS also typically suffer from one or more of about 17 neglected, but burdensome, tropical diseases often called "diseases of poverty" because they prey on the "bottom billion"—the world's poorest people. They include ailments such as trachoma, schistosomiasis, lymphatic filariasis, leishmaniasis, Chagas disease and onchocerciasis, all of which are either insect-borne disease, bacterial infections, or caused by parasitic worms.

Despite the illness and deaths attributable to these diseases, proposed US funding for fighting them was only about \$155 million in 2011, or about 3 percent of the \$5.6 billion invested in HIV/AIDS efforts. Moreover, the

programs often exist in isolation from one another with, for example, many programs restricting support only to antiretroviral drugs to treat AIDS.

Yet tropical disease experts note that in places like sub-Saharan Africa, where neglected diseases affect 1.4 billion people, co-infections with HIV are common. And they see mounting evidence that dealing with multiple diseases at the same time and in the same place is more cost-effective and clinically beneficial.

Walson pointed to a program in Western Kenya that focused on a community suspected of having high levels of HIV but whose remote location made it hard to reach to conduct testing. The program promised access to free bed nets and water filters to those residents who came in for a test. In just six days, some 10,000 residents turned out for the free nets and filters. The result: 1181 people were found to be HIV positive and referred to care while thousands of people gained new tools for preventing malaria and water-borne diseases.

In another example of the potential benefits of targeting multiple problems in a single intervention, a study initially focusing on treatment for onchocerciasis, a parasitic disease also known as river blindness, was broadened to offer insecticide-treated bed nets (ITNs), malaria drugs and vitamin A. The study, which covered an area with 2.35 million people, increased bed net coverage by nine-fold.

Sten Vermund, Professor of Pediatrics and Director of the Vanderbilt Institute for Global Health, noted the need to address any co-infections that might increase HIV viral load. He pointed to studies linking higher viral load with a higher likelihood of transmitting HIV, and a low load with reduced disease progression and HIV transmission risk. He said a review of a wide number of studies revealed that treating a variety of co-infections, including TB, malaria, schistosomiasis, filariasis, herpes, gonorrhea and syphilis decreased viral load to varying degrees.

"If de-worming efforts for neglected diseases reduces the viral load even just a little, then you could expect some benefit for preventing or slowing HIV transmission," said Vermund. "But it's also helpful to keep in mind that a majority of people don't know they have HIV. An effective mass de-worming campaign could have huge effects without even knowing the community's HIV status."

Peter Hotez, ASTMH President and founding dean of the National School of Tropical Medicine at Baylor College of Medicine, and Alan Fenwick, Professor of Tropical Parasitology and Director of Schistosomiasis Control Initiative at the Department of Infectious Diseases Epidemiology at Imperial College of London, offered a presentation focused on improved treatment for schistosomiasis. Schistosomiasis is a preventable, chronic, inflammatory condition caused by a parasite infection that is found in approximately 220 million people, most of whom live in sub-Saharan Africa. The parasite swims in water and burrows into human skin on contact. It is linked to an estimated 280,000 deaths each year. In women, the disease often affects the cervix and vagina where it can cause infertility, painful intercourse, and post-coital bleeding. One type of schistosomiasis known as female urogenital schistosomiasis affects girls and young women and is associated with HIV infection.

"These women are at highest risk of HIV infection and should be the focus of public health interventions," said Fenwick.

The high prevalence of urogenital schistosomiasis appears to be associated with higher rates of HIV and the genital lesions seen with this type of schistosomiasis may contribute to the acquisition of HIV in women. The researchers believe schistosomiasis interventions can be seen as a type of HIV/AIDS control, with mass treatment in girls aimed at preventing the onset of genital lesions.

In his President's address to the ASTMH meeting, Hotez challenged his colleagues to move beyond a focus on individual conditions to embrace a concerted campaign against the totality of tropical diseases. Referencing Bill Gates' call for adopting an "audacious goal" of eradicating malaria, Hotez called for expanding the "audacious goal" to ridding the world of all its neglected tropical diseases.

He portrayed neglected diseases as everyday manifestations of the Four Horsemen of the Apocalypse in that they cause pestilence, death, underlie famine and worsen the conditions of war. Hotez noted the importance of fighting disease to the success of international anti-poverty initiatives. "These diseases don't just occur in a setting of poverty; these diseases are a stealth cause of poverty in low and middle income countries," he said.

He quoted John Gardner, the Secretary of Health under President Lyndon Johnson, who said: "There are no better grounds on which we can meet other nations and demonstrate our own concern for peace and the betterment of mankind than in a common battle against disease."

In a separate presentation at ASTMH, Paul Farmer, founder of Partners in Health, also underscored the importance of attaching the fight against neglected diseases to a broader agenda.

"We need to understand the impact we can have when we link our understanding of improvements in people's lives to policy endeavors that can change the lives of millions," he said. "Often this does not happen."

The question is how can we build consensus in the scientific community and among our allies; how can we build coalitions to pull those policy levers more effectively? All of the diseases that affect the poor are neglected."

*Provided by American Society of Tropical Medicine and Hygiene*

<http://nyti.ms/tfYM9R>

## **Physicists Anxiously Await New Data on 'God Particle'**

***Lisa Randall, a Harvard particle theorist and the author of "Knocking on Heaven's Door," is watching for the latest on the Higgs boson.***

**By DENNIS OVERBYE**

High noon is approaching for the biggest manhunt in the history of physics. At 8 a.m. Eastern time on Tuesday morning, scientists from CERN, the European Center for Nuclear Research, are scheduled to give a progress report on the search for the Higgs boson — infamously known as the “God particle” — whose discovery would vindicate the modern theory of how elementary particles get mass.

The report comes amid rumors that the two competing armies of scientists sifting debris from hundreds of trillions of proton collisions in CERN’s Large Hadron Collider, or L.H.C., outside Geneva, have both finally seen hints of what might turn out be the elusive particle when more data is gathered next year.

Alternatively, the experimentalists say that a year from now they should have enough data to rule out the existence of the most popular version of the Higgs boson, sending theorists back to their blackboards in search of another explanation of why particles have mass.

So the whole world will be watching.

Among them will be Lisa Randall, a Harvard particle theorist and author of the new book “Knocking on Heaven’s Door: How Physics and Scientific Thinking Illuminate the Universe and the Modern World.” In an interview with Dennis Overbye of The Times, Dr. Randall provided this guide to the action for those of us in the bleachers.

### **Q. What is the Higgs and why is it important?**

**A.** The name Higgs refers to at least four things. First of all, there is a Higgs mechanism, which is ultimately responsible for elementary particles’ masses. This is certainly one of the trickier aspects of particle physics to explain, but essentially something like a charge — not an electric charge — permeates the vacuum, the state with no particles.

These “charges” are associated with a Higgs field. As particles pass through this field they interact with the “charges,” and this interaction makes them act as if they had mass. Heavier particles do so more, and lighter particles do so less. The Higgs mechanism is essential to the masses of elementary particles.

The Higgs particle, or Higgs boson, is the vestige of the simplest proposed model of what created the Higgs field in the first place. Contrary to popular understanding, the Higgs field gives mass — not the Higgs boson. But a discovery of the Higgs boson would tell us that the Higgs mechanism is right and help us pin down the theory that underlies both the Higgs mechanism and the Standard Model.

In the simplest implementation of the Higgs mechanism, the experimental consequence is the Higgs boson. It is the particle that the experimentalists are now searching for.

Of course, Higgs is also the name of the person, Peter Higgs, who first developed the underlying theory (along with five others who will be in contention for the Nobel Prize if and when the Higgs particle is discovered.)

### **Q. How will we know it when we find it?**

**A.** In the simplest implementation of the Higgs mechanism, we know precisely what the properties of the Higgs boson should be. That’s because of its connection to the Higgs mechanism, which tells us that its interactions with any particular particle are determined by that particular particle’s mass.

Knowing the interactions, we can calculate how often the Higgs boson should be produced and the ways in which it should decay. It can decay only into those particles that are light enough for energy to be conserved. Roughly speaking, the Higgs boson decays into the heaviest such particles the most often, since it interacts with them the most strongly.

What we don’t know, however, is the Higgs boson’s mass. The Higgs boson decays differently, depending on its mass, since a heavier Higgs boson can decay in ways that a light Higgs boson can’t. So when experimenters look for the Higgs boson, they look over a range of masses and employ a variety of search strategies.

### **Q. What do we know about it so far?**

**A.** Experimenters have already ruled out a large range of masses. The Higgs boson, if it exists, has to be heavier than 114.4 giga-electron volts (GeV), which are the units of mass that particle physicists use. By comparison, protons, the bedrock of ordinary matter, are about 1 giga-electron volt, and an electron is only half a million electron volts.

Based on recent searches by the L.H.C., the Higgs boson is also excluded between about 140 GeV and 500 GeV. This makes the most likely region for the Higgs mass to be between about 115 and 140 GeV, which is the range Tuesday's results should focus on, although in principle heavier Higgs boson masses are in contention too.

I don't want to shatter hopes, but don't count on Tuesday's results being definitive. This is the toughest range of masses for the L.H.C., and detection is tricky for this range. I suspect they will have enough evidence not to exclude the Higgs, but too little to fully pin it down without next year's data.

**Q. What difference does its mass make?**

**A.** Actually, as far as matter's properties go, it doesn't really make a great deal of difference. As long as the Higgs mechanism is in place, elementary particles that we know about will have the masses that they do.

But no one thinks the Higgs is the final word about what underlies the Standard Model of particle physics, the theory that describes the most basic elements of matter and the forces through which they interact. Even if the Higgs boson is discovered, the question will still remain of why masses are what they are.

According to quantum field theory — the theory that combines quantum mechanics and special relativity — masses would be expected to be ten thousand trillion times bigger. Without some deeper ingredient, a fudge of that size would be required to make it all hang together. No particle physicist believes that.

We all expect a richer theory underlying the Standard Model. That's one reason the mass matters to us. Some theories only accommodate a particular range of masses. Knowing the mass will give us insight into what that deeper underlying theory is.

**Q. Is the L.H.C. a flop if we don't find the Higgs boson?**

**A.** The great irony is that not finding a Higgs boson would be spectacular from the point of view of particle physics, pointing to something more interesting than the simple Higgs model. Future investigations could reveal that the particle playing the role of the Higgs has interactions aside from the ones we know have to be there for particles to acquire mass.

The other possibility is that the answer is not the simple, fundamental particle that the Large Hadron Collider currently is looking for. It could be a more complicated object or part of a more complex sector that would take longer to find.

**Q. Does this have anything to do with neutrinos — specifically, the ones that were recently reported as having traveled faster than light on a journey that originated at CERN?**

**A.** Neutrinos have tiny masses. The Higgs mechanism is probably partially responsible for those, too. Just nothing that encourages them to go faster than light (which they most likely don't). In 1993, the U.S. Congress canceled a larger American collider, the superconducting super collider, which would have been bigger than the CERN machine.

**Q. Would it have found the Higgs particle years ago?**

**A.** Yes, if it had gone according to schedule. And it would have been able to find things that weren't a simple Higgs boson, too. The L.H.C. can do such searches as well, but with its lower energy the work is more challenging and will require more time.