

## **Prion disease diagnosis just got easier**

### ***Test for Creutzfeldt-Jakob disease raises hopes of speedier diagnosis.***

**By Tiffany O'Callaghan**

Invasive biopsy is currently the only sure way to diagnose the degenerative neurological condition Creutzfeldt-Jakob Disease (CJD). But a highly sensitive assay could change that, providing a fast, accurate alternative for early diagnosis of this rare but deadly condition.

In its most common form, known as sporadic CJD, the disease affects roughly one in a million people. Beginning in the 1990s, several cases of a variation of CJD known as vCJD were reported among people who had consumed beef from cows infected with another disease, bovine spongiform encephalopathy (BSE).

The findings, published online in *Nature Medicine*, also suggest that the assay-developed by microbiologist Ryuichiro Atarashi of Nagasaki University, Japan, and his team-could pave the way for the screening of broad sectors of the population.

CJD is a prion disease, in which an isomer of a common protein known as the prion protein (PrP) takes on an abnormal shape and becomes an infectious variant called PrP<sup>Sc</sup>. This variant is thought to trigger the subsequent malformation of other PrP proteins. Unlike their normal counterparts, PrP<sup>Sc</sup> prions cannot be broken down, and instead accumulate-often clustering in brain tissue.

The pockets of abnormal tissue that result cause brain tissue to develop a sponge-like appearance, and because prion conditions can be spread by affected humans or animals, the diseases are often referred to as transmissible spongiform encephalopathies (TSEs). Humans can be affected by several such conditions, while in addition to BSE in cows, there are several other such disorders among animals, including a condition called scrapie in sheep and hamsters.

#### **No false positives**

One problem that has plagued developers of non-biopsy diagnostic techniques is that it is often difficult to avoid false positives among samples taken from patients with neurodegenerative disorders other than CJD.

So Atarashi and his colleagues used a new assay known as a real-time quaking-induced conversion (RT-QUIC) assay. "Quaking-induced" refers to in vitro shaking, which researchers believe helps to accelerate the reactions, enabling the assay to produce results more quickly.

The team tested cerebrospinal fluid samples from 18 people with CJD and 35 people with other neurodegenerative diseases. This pilot group produced no false positives, and CJD was correctly diagnosed more than 83 percent of the time. The researchers compared these results with those obtained using an existing assay that tests for levels of a protein known as 14-3-3, which is a marker for sporadic CJD. When tested on patient samples, the accuracy of 14-3-3 was 72.2 percent, whereas the specificity was 85.7 percent.

In a subsequent blind trial on 30 cerebrospinal fluid samples from Australia, RT-QUIC showed 100 percent specificity, resulting in no false positives among the 14 control samples, and correct diagnoses of 87.5 percent. 14-3-3 was equally accurate, but the rate of false positives was much higher.

"This technique allows definitive ante-mortem confirmation of CJD," says Atarashi, adding that this is currently difficult because it demands the detection of PrP<sup>Sc</sup> in patients' biopsy specimens.

#### **Supersensitivity**

The RT-QUIC assay is also extraordinarily sensitive-detecting the presence of harmful prions at very high dilutions-and speedy, yielding results within 48 hours. Atarashi first began developing RT-QUIC as a researcher at the National Institute of Allergy and Infectious Diseases, Rocky Mountain Laboratories, in Montana. In 2008, he and his team successfully used it to screen cerebrospinal fluid taken from scrapie-infected hamsters. In December, Atarashi co-authored a paper reporting the efficacy of the RT-QUIC assay on nasal secretions and cerebrospinal fluid from hamsters with prion disorders.

Byron Caughey, chief of prion/TSE research at the Rocky Mountain lab and a co-author of the two hamster studies, is encouraged by the application of the assay to human cerebrospinal fluid samples. "Of course it will also be important to detect prion diseases in other species, but human diagnosis is of pre-eminent importance," Caughey says.

And although the next step is to replicate the findings in a much larger sample, the promise shown by RT-QUIC in analyzing substances other than spinal fluid in hamsters suggests a potentially fertile area for future research in humans. If RT-QUIC could be used to screen blood samples, or cheek or nasal swabs, for example, it could open up the possibilities of much earlier diagnosis and more widespread screening of donated blood.

"The earlier you're able to detect the presence of an infection in humans or animals, the more chance you have of preventing transmission to others and treating the disease in those who are infected," Caughey says.

## **Pakistan floods last summer could have been predicted**

**WASHINGTON - Five days before intense monsoonal deluges unleashed vast floods across Pakistan last July, computer models at a European weather-forecasting center were giving clear indications that the downpours were imminent.**

Now, a new scientific study that retrospectively examines the raw data from these computer models, has confirmed that, if the information had been processed, forecasters could have predicted extremely accurate rainfall totals 8-10 days beforehand. The study also finds that the floods themselves could have been predicted if this data, which originated from the European Centre for Medium-Range Weather Forecasting (ECMWF), had been processed and fed into a hydrological model, which takes terrain into account.

The July floods killed thousands of people and tens of thousands of cattle, and left large parts of Pakistan in shambles. The waters displaced, or disrupted the lives of, an estimated 20 million people.

"People don't understand the powers of modern environmental prediction," says Peter Webster, a professor of earth and atmospheric science at the Georgia Institute of Technology in Atlanta and lead author of the new study. "This disaster could have been minimized and even the flooding could have been minimized. If we were working with Pakistan, they would have known 8 to 10 days in advance that the floods were coming."

He and his colleagues report their findings in a paper accepted for publication in *Geophysical Research Letters*, a journal of the American Geophysical Union.

The ECMWF, a London-based organization of 33 participating European countries, "does not give out weather forecasts and weather warnings to the general public or media," notes ECMWF scientist Anna Ghelli. "ECMWF provides numerical forecasts to its member and co-operating states and they are responsible to prepare forecasts for the public and advise the authorities in their own countries."

"We noticed that the signal was there five days in advance," Ghelli recalls. However, the lack of a cooperating agreement between the forecasting center and Pakistan meant that these rainfall warnings didn't make it to the Pakistani people, nor did Pakistan's own meteorological agency forecast the flooding.

In their research, the Georgia Tech meteorologists use data from the European center to analyze whether or not the rainfall was above average for Pakistan and if the huge surges in the Indus River would have been predictable if flood forecasters were monitoring the country. They determine that, while the rainfall total for 2010 was slightly above average for the region, the July deluges were exceptionally rare, with rainfall amounts exceeding 10 times the average daily monsoon rainfall. They also find that if a flood forecasting model had been in place, the floods would have been predicted in time to issue warnings.

As a result of processing the raw output from ECMWF models from before the Pakistani deluge, the team achieves greater accuracy than the raw numerical forecasts alone provided. Some weather stations in Pakistan recorded nearly a foot (30 centimeters) of rainfall during the 4-day downpour. The after-the-fact predictions by Webster and his colleagues came in slightly below those amounts at the same locations.

Webster says that processing raw data into weather forecasts and combining them with hydrological models is only half the work. In order to have any effect, the resulting flood forecasts must be successfully disseminated at the village level, and local leaders must also understand them.

In nearby Bangladesh, Webster spent five years creating a flood-forecasting technique and organizing a cooperating agreement with the Georgia Institute of Technology, ECMWF, the Asian Disaster Preparedness Center and the government of Bangladesh. When flooding occurred there several years ago, warnings made possible by the forecasting pact not only averted loss of life, but also saved residents as much as \$450 per farm – about the equivalent of an average annual salary in that country.

In a few weeks, Webster will attend an international meeting of developing nations in Bangkok to build support for flood forecasting in Pakistan. He says a forecasting system in Pakistan would cost a few million dollars to set-up, but as little as \$100,000 a year once operational. He hopes to convince the World Bank, currently providing \$1 billion of flood-recovery financing to Pakistan, to fund the project.

In Bangladesh, Webster recalls, an imam at a local mosque told him about how they discussed the flood forecasts each day in prayer. This is the sort of local solution that Webster envisions for Pakistan as well.

*The National Science Foundation funded this research. Notes for Journalists*

*As of the date of this press release, the paper by Webster et al. is still "in press" (i.e. not yet published). Journalists and public information officers (PIOs) of educational and scientific institutions who have registered with AGU can download a PDF copy of this paper by clicking on this link: <http://www.agu.org/journals/pip/gl/2010GL046346-pip.pdf> Or, you may order a copy of the paper by emailing your request to Peter Weiss at [pweiss@agu.org](mailto:pweiss@agu.org) or Maria-José Viñas ([mjvinas@agu.org](mailto:mjvinas@agu.org)). Please provide your name, the name of your publication, and your phone number. Neither the paper nor this press release are under embargo. Title: "Were the 2010 Pakistan floods predictable?" Authors: Peter J. Webster, V.E. Toma and H-M Kim: School of Earth and Atmospheric Science, Georgia Institute of Technology, Atlanta, Georgia.*

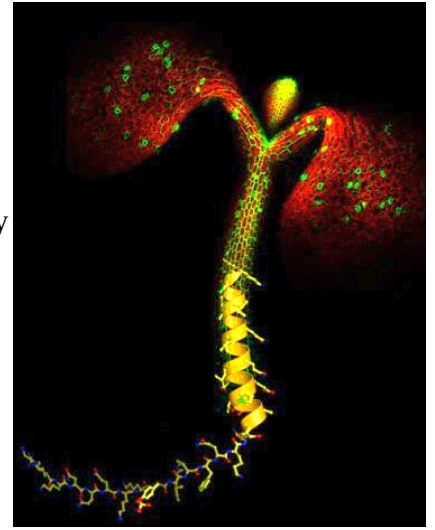
## Different evolutionary paths lead plants and animals to the same crossroads

**LA JOLLA, CA - In analyzing the molecular sensor for the plant growth hormone brassinolide, researchers at the Salk Institute for Biological Studies discovered that although plants took an evolutionary path different from their animal cousins, they arrived at similar solutions to a common problem: How to reliably receive and process incoming signals.**

The team's findings, published in the February 1, 2011 issue of *Genes and Development*, revealed that so-called tyrosine phosphorylation - used as an "on" or "off" switch and long thought to be a feature unique to animal cells - is a mechanism conserved across the animal and plant kingdoms.

"There seem to be only so many ways to build a robust signaling system," says Howard Hughes Medical Institute investigator Joanne Chory, Ph.D., professor and director of the Plant Molecular and Cellular Biology Laboratory and holder of the Howard H. and Maryam R. Newman Chair, "and plants and animals have hit upon the same mechanisms."

As different as they may seem, both mammalian and plant cells need to be able to perceive small molecule hormones to respond to changes in the environment. While human cells draw on a wide variety of sensor molecules, including more than 800 different G-protein-coupled receptors, 48 known nuclear hormone receptors and 72 receptor kinases, plants rely mostly on the latter.



***Despite their divergent evolutionary history, membrane-bound kinase receptors in animals and plants rely on similar regulatory mechanisms to control their activity.*** Image: Courtesy of Yvon Jaillard, Michael Hothorn and Jamie Simon, Salk Institute for Biological Studies

"This group of receptors is by far the largest one in plants," says postdoctoral researcher and co-first author Michael Hothorn, "but we don't know much about the activation mechanism apart from 'there's a bunch of new phosphorylations.'"

Kinases transfer phosphate groups to proteins and come in two principal flavors: They either attach the phosphate group to the amino acid tyrosine within the protein or to serine or threonine. The vast majority of receptor kinases in animals possess tyrosine kinase activity, while only a few are specific for serine-threonine.

With the exception of a small handful of dual-specificity kinases, all plant receptor kinases have been pegged as serine-threonine kinases. One of few known outliers is the receptor for brassinolide, a key element of plants' response to light. "Binding of brassinolide to its receptor allows plants to adjust growth when they need to outcompete their neighbors to reach more light or water," explains postdoctoral researcher and co-first author Yvon Jaillais. "But at the same time the receptor needs to be tightly regulated so plants don't waste their resources when they don't have to."

The brassinolide receptor BRI1 is kept in a relatively inactive state by its intracellular tail and a small inhibitory protein known as BKI1. Based on earlier studies in Chory's lab, the Salk researchers knew that autophosphorylation of the receptor was necessary, but what triggered the release of the inhibitory protein remained unclear.

In an effort to understand the activation mechanism, the Salk researchers discovered that BKI1 acts through two evolutionarily conserved motifs: a 20-amino-acid sequence that binds the receptor kinase domain and a lysine-arginine-rich motif that anchors the inhibitory peptide to the plasma membrane. Phosphorylation of a key tyrosine within the membrane-targeting motif releases BKI1 from the membrane, relieving kinase inhibition and allowing the formation of an active signaling complex.

The phosphorylation of BKI1 is not only the first documented example of tyrosine transphosphorylation in plants, the underlying principle also closely resembles the mechanism used by bona fide receptor tyrosine kinases to regulate their activity. "Plant and animal receptor kinases evolved independently, yet their activation relies on similar mechanisms," says Chory. By defining common features in plant and animal receptor signaling pathways, the Salk researchers hope to learn more about what the requirements for a robust signaling system are. Although plants don't encode canonical tyrosine kinases in their genomes, tyrosine phosphorylation will emerge as an important topic in plant signaling, predicts Hothorn.

*Researchers who also contributed to the work include Yousseff Belkhadir and Tsegaye Dabi in the Plant Biology Laboratory at the Salk Institute, as well as Zachary L. Nimchuk and Elliot Meyerowitz in the Division of Biology at the California Institute of Technology in Pasadena, California.*

The work was funded in part by the Howard Hughes Medical Institute, the National Institutes of Health, the National Science Foundation, the European Molecular Biology Organization, the International Human Frontier Science Program Organization, the Life Sciences Research Foundation, and the Marc and Eva Stern Foundation.

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## **Dogs can accurately sniff out early stage bowel cancer**

### ***Colorectal cancer screening with odor material by canine scent detection***

Dogs can sniff out bowel cancer in breath and stool samples, with a very high degree of accuracy - even in the early stages of the disease - reveals research published online in the journal Gut.

The findings prompt the authors to suggest that chemical compounds for specific cancers circulate throughout the body, which opens up the prospect of developing tests to pick up the disease before it has had the chance to spread elsewhere.

A specially trained Labrador retriever completed 74 sniff tests, each comprising five breath (100 to 200 ml) or stool samples (50 ml) at a time, only one of which was cancerous, over a period of several months.

The samples came from 48 people with confirmed bowel cancer and 258 volunteers with no bowel cancer or who had had cancer in the past.

Around half of the volunteer samples came from people with bowel polyps, which although benign, are considered to be a precursor of bowel cancer. And 6% of the breath samples and one in 10 of the stool samples from this group came from those with other gut problems, such as inflammatory bowel disease, ulcers, diverticulitis, and appendicitis.

The bowel cancer samples came from patients with varying stages of disease, including early stage.

The dog successfully identified which samples were cancerous, and which were not, in 33 out of 36 breath tests and in 37 out of 38 stool tests, with the highest detection rates among those samples taken from people with early stage disease. This equates to 95% accuracy, overall, for the breath test and 98% accuracy for the stool test, compared with conventional colonoscopy - a procedure involving a tube with a camera on the end inserted through the back passage.

Samples from smokers or from those with other types of gut problems, which might be expected to mask or interfere with other smells, did not pose a problem for the dog. This indicates that there are specific discernible odours given off by cancer cells which circulate around the body, say the authors. And it is backed up by other research and anecdotal evidence indicating that dogs can sniff out bladder, skin, lung, breast and ovarian cancers, they add. The authors concede that using dogs to screen for cancers is likely to be impractical and expensive, but a sensor could be developed to detect the specific compounds.

The faecal occult blood test, which picks up hidden blood in a stool sample is an effective and non-invasive method of screening for bowel cancer, say the authors, but it is only able to pick up early stage disease in one in 10 cases. "Early detection and early treatment are critical for the successful treatment of cancer and are excellent means for reducing both the economic burden and mortality [of bowel cancer]," comment the authors.

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## **Boys will infect boys, swine flu study shows**

### ***Boys predominantly pass on flu to other boys and girls to girls, according to a new study of how swine flu spread in a primary school during the 2009 pandemic, published today in the journal Proceedings of the National Academy of Sciences.***

The results also suggest that flu transmission is most intensive between children of the same class, but that sitting next to an infected person does not significantly increase a child's risk of catching flu. The data will help researchers to model how epidemics spread and how interventions such as school closures can help contain an outbreak. In the study, researchers from Imperial College London, the US Centers for Disease Control and Prevention (CDC) and the Pennsylvania Department of Health analysed how social networks influenced the spread of H1N1 pandemic flu in an elementary school in Pennsylvania.

The results show that children are about three times more likely to transmit flu to children of the same gender than to children of the opposite gender. The researchers also found that the transmission rate is about five times higher between classmates than between children in a different class in the same grade, and about 25 times higher than between children in different grades. However, sitting next a child with flu does not significantly raise a child's risk of catching it.

The study involved 370 pupils (81 per cent of children in the school) from 295 households. The researchers collected extensive data from seating charts, school timetables, bus schedules, nurse logs, attendance records and questionnaires. Although it is impossible to determine exactly who caught flu from whom, the researchers used sophisticated statistical methods to probabilistically reconstruct the pattern of spread and estimate the rates of transmission in different settings.

"Mathematical models are useful for predicting how outbreaks will spread, but in order to make the models accurate, we need to supply them with data about how disease spreads in the real world," said Dr Simon Cauchemez, the lead author of the study from the Medical Research Council Centre for Outbreak Analysis and Modelling at Imperial College London. "This is one of the most comprehensive studies to date on how a flu epidemic spreads between children in school, and it tells us a great deal about how social networks influence transmission.

"The data from this study will help us make more accurate models, which can help public health officials to handle epidemics effectively. For example, these new models could help us better understand whether and when it would be appropriate to close a school, or whether it might be better to close individual classes or grades."

The school that was studied in this project closed 18 days after the outbreak began, when 27 per cent of pupils had already shown symptoms. According to the analysis, transmission rates were falling at this stage, and closing the school probably had little impact on the spread of the epidemic.

Dr David Swerdlow, Senior Advisor for Epidemiology and Emergency Response, National Center for Immunization and Respiratory Diseases, at the CDC, said: "This was a unique opportunity at the inception of the 2009 influenza A (H1N1) pandemic to learn about transmission in social networks. The investigation demonstrates the benefits of partnerships as the collaboration included Imperial College London, the Pennsylvania Department of Health, and CDC."

*The study was funded by the Medical Research Council, the Bill and Melinda Gates Foundation, the NIGMS MIDAS initiative, the EU FP7 FluModCont project, Research Councils UK, Pennsylvania Department of Health, and the CDC.*

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### **Specific populations of gut bacteria linked to fatty liver**

#### **Findings point to digestive bacterial influence on choline metabolism**

The more we learn about biology, the closer we get to being able to treat disease – and the more complicated our understanding of disease itself becomes.

A new research finding showing a strong relationship between complex microbial ecologies in human intestines and the common but serious medical condition known as fatty liver illustrates this paradox.

From past genomic studies, we have learned that a mind-boggling multitude of different kinds of benign bacteria inhabit our intestines and that these populations can vary almost infinitely from one human being to the next. We know that the kind of food we eat is important to our health and we know that having the right bacteria in our intestines is important in digesting our food properly, but we still do not know how our individual variations in gut bacteria might influence more specific health issues. In particular, we do not know how these bacteria influence how the substances we eat affect our organ systems.

In the condition known as fatty liver, fat deposits build up in the liver, with potentially serious health consequences for nearly a third of the American population. Fatty liver can be caused by alcohol abuse, obesity, hormonal changes and/or diabetes. Recent work has suggested that diet is also important with strong indications that deficiencies in the essential nutrient choline might be partially involved in some incidences of the condition. Choline deficiency also implicates genetics, since many people lack the genes to efficiently make choline internally.

Now, a new bioinformatics finding shows that the abundance or scarcity of certain types of bacteria in the gut may also help predict susceptibility to non-alcoholic fatty liver. The implication of the finding is that these groups of bacteria may be influencing the body's ability to properly use the choline available in food, though the study does not examine the specific metabolic activity of the bacteria involved.

In a metagenomic analysis of the microbial communities living in the intestinal tracts of 15 female patients participating in a study of the effects on liver condition from a choline-depleted diet, bioinformatics researchers at the University of North Carolina at Charlotte found a strong correlation between the relative abundances of two specific classes of bacteria and the development of fatty liver. A report on the finding appears in the current issue of the journal *Gastroenterology*.

"Certain bacterial populations correlated very strongly with increased fat in the liver during a restricted choline diet," said Melanie Spencer, a doctoral student in bioinformatics at the University of North Carolina at Charlotte and the lead author on the paper. "To us, it's an amazing result because you just don't see this clear a correlation in biological experiments in humans very often."

The authors on the paper are Spencer, Anthony Fodor, Timothy Hamp and Robert Reid from the department of bioinformatics and genomics at UNC Charlotte, as well as Steven Zeisel and Leslie Fischer from the department of nutrition at the University of North Carolina at Chapel Hill.

Using a metagenomic technique that compares versions of a ribosomal RNA gene known to vary between bacterial groups, the researchers analyzed the genomes of the patients' gut bacteria before, during and after the patients were put on a choline deficient diet. Because all patients consumed identical diets during the study, the researchers predicted that the initially distinct and complex communities of microbes in the patients' intestinal tracts would react by becoming less distinct from each other. The researchers found instead that, though each of the patients' bacterial communities did change a bit, each individual's community still remained distinctive throughout the study.

"What we expected we might find would be that when we put the patients on exactly the same diets, everyone's gut microbe mixture would begin to look similar, with the microbial communities converging. It did not happen – everybody was clearly individual throughout the entire study," Spencer noted. "So we also looked at how the patients' microbes actually changed in pattern, even though they remained distinct from each other," she said. "The patterns of change were very interesting. Some of the patterns were very distinct in themselves."

The researchers noticed that among the numerous classes of bacteria present in each patient, variations in the populations of two particular groups seemed to correspond with variations between patients in the degree to which they developed a fatty liver during the period of dietary choline depletion.

"Those patients with the highest abundance of Gammaproteobacteria at the beginning of the study seemed to have the lowest fatty liver development. The ones with the least developed the most fatty liver," Spencer noted. "Erysipelotrichi showed exactly the opposite association, though this relationship was not quite as strong. So there seemed to be change going on in opposite directions."

When the trends of Gammaproteobacteria abundance and Erysipelotrichi scarcity were combined and related to fatty liver development, the relationship became even stronger.

Finally, the researchers factored in individual genetic variations that affect internal production of the nutrient choline and that should explain why some patients developed fatty liver and others did not. Surprisingly, the results showed that each person's genetics did not entirely account for their fatty liver outcome. When the researchers modified the analysis to include the abundances of the two bacterial groups and each individual's genetics, the correlation between fatty liver development and these three factors was nearly perfect. Further mathematical tests were performed to show that the correlations were not likely to be an artificial result of some bias hidden in the analysis.

"There was some concern that we were 'over-fitting' the model," Spencer noted, "so we tested it out and ran a million permutations, altering the bug abundance and subject association, to see if we could identify how many actually showed a higher correlation by chance. What we found is that the p values still held up. We can have a lot of confidence in the result."

The big question that remains for the team is why the two bacterial populations correlate so strongly to the development of fatty liver. Anthony Fodor, UNC Charlotte assistant professor of bioinformatics and the project's director, sees a possible explanation, while warning against drawing specific conclusions without further study. "We cannot yet assign cause and effect, but it implies that some bacteria are doing something that is making it easier for people to deal with a choline deficiency and for the liver to metabolize fat."

Conversely, the bacteria whose high population levels correlate with disease may be somehow removing available forms of choline from digested food. Fodor explains that further study will be needed to answer those questions. "We're debating what the next step is," he said. "In some ways, this is a very specialized experiment because we are inducing fatty liver in a very specific way. In the general population, fatty liver is induced in many, many ways and not everyone who has fatty liver has low choline.

"It's probably like Alzheimer's or cancer, where there are many different causes for a disease that displays a common phenotype. More research will be required to determine the extent to which bacterial populations play a role in fatty liver development in the general population, but our results strongly suggest that there may be a link in some people."

*The article is available online at [http://www.gastrojournal.org/article/S0016-5085\(10\)01739-7/fulltext](http://www.gastrojournal.org/article/S0016-5085(10)01739-7/fulltext) (fee required for access) or contact [jbhathaw@uncc.edu](mailto:jbhathaw@uncc.edu) for a copy.*

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### **Researchers bust bat rabies stereotype**

#### ***Rabies rate in bats not as high as estimates suggest***

Bats tend to have a bad reputation. They sleep all day, party at night, and are commonly thought to be riddled with rabies. A study by University of Calgary researchers has confirmed that bats are not as disease-ridden as the stigma suggests.

"The notion that bats have high rates of rabies is not true," says Brandon Klug, a graduate student at the University of Calgary and the lead author of a paper published in the Journal of Wildlife Diseases.

"Those of us that work with bats have always known the rates are low; and now we have evidence that bats aren't disease-ridden vermin their reputation would have you believe."

Previous studies have suggested that typically about 10 per cent of bats taken by the public to be tested have the disease and prevalence varies greatly, depending on the species and how often that species is around people. But University of Calgary research says the number is closer to one per cent regardless of species or where the bats roost.

Researchers compared bats turned in by the general public and those randomly sampled from their natural environment. In the field, they looked for the disease in carcasses of migratory tree-roosting hoary bats (*Lasiurus cinereus*) and silver-haired bats (*Lasionycteris noctivagans*) killed by wind turbines. These species are among bat species with the highest reported prevalence of rabies in North America. At the same time they compared these bats with rabies prevalence from literature contained in public health records in North America.

"This study is significant because it confirms that rabies rates for bats has been over-estimated. It's also the first time such a rigorous literature review has been completed on this topic," says co-author Dr. Robert Barclay, biological science professor and head of the Department of Biological Sciences at the University of Calgary.

University of Calgary researchers sent 217 carcasses to the Centers of Disease Control and Prevention in the U.S for testing. They also reviewed the literature on reported rabies in multiple bat species in North America covering the past 56 years, which included 65,096 bats.

Bats, along with other species including foxes, skunks and raccoons, are considered reservoirs for the disease. Rabies is passed from bat to bat at a rate that keeps the virus in the population, but rarely fast enough to eradicate the bat population or slow enough to result in the demise of the virus.

"Since the background rabies rate in bats is low, less than one percent, people should focus more on the ecosystem services they provide without worrying that every other bat has rabies. This is especially important right now because bats are facing some heavy threats, like wind turbines and white nose syndrome," says Klug.

"With that said, healthy bats normally don't come in contact with people, so those that do are more likely to be sick, so we're not encouraging people to go out and handle them."

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### **An Olympic gold medal costs a government \$55 million**

***In order to arrive at this result the researchers calculated the price with a model that measures the number of medals according to government expenditure in sport, along with other variables.***

"This model allows accurate measurement of how much extra expense is necessary to win each medal," the UC3M professors Juan de Dios Tena and Ramón J. Flores explained, who carried out this study within the Sports Economics Research Group, headed by professor David Forrest, of the University of Salford (England) and which also includes Ismael Sanz from the Universidad Rey Juan Carlos and Jaime Álvarez from Universidad Complutense of Madrid. "We have estimated the relation between this expenditure and Olympic success once relevant economic, political, and demographic variables are taken into account, such as the size of the country," Tena pointed out. This study was presented at the workshop "The Economic of the Olympic Games" at Groningen in July of 2008, entitled "Can governments buy Olympic medals?" and at present is in the revision process for publication in a research journal.

In the area of Sport Economics these researchers use econometric models (usually regression models) to analyze sports phenomena in which there are economic determinants. The basic general idea is that there are many possible causes for a phenomenon. "A regression model offers an estimate of the individual effect of each of these causes, once the others are controlled for", explained professor Flores, which allows him to draw rigorous conclusions from the statistics models that can thus determine the concrete influence of an element within the context of sport.

### **The dilemma of sacking a coach**

In the case of football teams, for example, this research group has analyzed the figure of the technical trainer and discovered that the effect of sacking a coach during the season is more negative than positive when this situation happens more than once. "Changing coaches reduces by half the number of points obtained in the next eight games for a unit," he remarked.

Based on the results obtained during several seasons by the clubs in the Argentinean league, the econometric model that they have developed shows an inverse relation between the number of sackings and team results. In a nutshell, the more sackings, the worse results in the middle term. "Similar studies carried out in European leagues, where the number of sackings is lower, does not show such an effect, suggesting that abusing the number of sackings can generate negative consequences within this context," concluded these UC3M Statistics Department professors.

Another subject related to the researchers' work is the effect that the 1995 Bosman Law has had on competitiveness in the most important football leagues. Before that law, in national competitions there was a very strict limitation governing the number of foreign players which could be signed on by each team, resulting in the available top foreign players usually going to the bigger clubs. With the new legislation eliminating this limitation, the number of players available greatly increased, so that the low and mid level clubs were also able to become stronger and increase their level as well as in tournament play. "In order to measure this increase we use measurements known in the literature, such as the percentage of points over the total obtained by the top two, four or ten teams in the league, as well as taking into account other factors which influence in the modification of the market, such as getting into Champions League and its resulting benefits," they noted. The conclusion after the Bosman Law came into effect is that the ratio of points of the top two teams decreased by 2 percent and by 4 percent for the top eight teams.

This type of data and research can serve to orient and aid in the decision-making process. In addition, the answers obtained can be extrapolated to wider contexts. "Our intention is to apply them profusely, and to collaborate in resolving issues which generate debate in society, and which produce interesting conclusions. These matters are rarely studied with the rigor that they deserve," asserted these professors from the UC3M Colmenarejo campus, who have the impression that in this area, work is presented as an "analysis" which scarcely goes beyond mere opinion. "Due to the media nature of anything related to sport, there are often statistical studies of low quality or which are carried out directly by fans and obtained by unscientific methods from samples which are not at all reliable."

[http://www.eurekalert.org/pub\\_releases/2011-01/foas-mta013111.php](http://www.eurekalert.org/pub_releases/2011-01/foas-mta013111.php)

**More than allergies: Histamine may be a possible drug target for multiple sclerosis**  
***New research published in the Journal of Leukocyte Biology suggests that histamine plays an important role as an immune modulator, which could be a significant finding for multiple sclerosis research***

If you think histamines are your nemesis during allergy season, here's something that might change your perspective. New research published in the Journal of Leukocyte Biology (<http://www.jleukbio.org>) shows that histamine could be an important molecule to developing new treatments for multiple sclerosis (MS). In the study, the scientists analyzed the role of histamine in an animal model of multiple sclerosis and found that histamine plays a critical role in preventing MS or lessening its effects.

"We hope that our study will help design new therapies for autoimmune diseases and in particular MS, for which there is still not a definitive cure," said Rosetta Pedotti, MD, Ph.D., a researcher involved in the work from the Neuroimmunology and Neuromuscular Disorders Unit at the Neurological Institute Foundation Carlo Besta in Milan, Italy.

Histamine is a neurotransmitter involved in allergic reactions and other physiological and pathological processes. It is best known for the role it plays in hypersensitivity reactions like allergies, and it generally works by dilating blood vessels and making vessel walls permeable so immune cells can move more easily.

Scientists studied the direct effects of histamine and two similar molecules that bind specifically on histamine receptors 1 or 2. Using a mouse model of MS, researchers generated MS-causing T lymphocytes and then treated these cells with histamine or the two other molecules. The effects of these treatments were evaluated by T cell functions analysis including proliferation, cytokine production, intracellular signaling pathways activation, and adhesion to brain vessels.

Results showed that histamine reduces the proliferation of myelin autoreactive T lymphocytes and the production of interferon-gamma, a crucial cytokine involved in brain inflammation and demyelination. Additionally, histamine reduced the ability of myelin autoreactive T cells to adhere to inflamed brain vessels, a crucial step in the development of MS.

"This research is very exciting for several reasons. First, it points to unexpected connection between pathways involved in autoimmunity and allergy and suggests previously unrecognized connections between these very different types of immune responses. Second, while extending studies in animal models such as these to humans takes substantially more work, these new data point to a potentially novel drug target for MS and possibly other autoimmune or central nervous system diseases," said John Wherry, Ph.D., Deputy Editor of the Journal of Leukocyte Biology.

*Details: Marilena Lapilla, Barbara Gallo, Marianna Martinello, Claudio Procaccini, Massimo Costanza, Silvia Musio, Barbara Rossi, Stefano Angiari, Cinthia Farina, Lawrence Steinman, Giuseppe Matarese, Gabriela Constantin, and Rosetta Pedotti. Histamine regulates autoreactive T cell activation and adhesiveness in inflamed brain microcirculation. J Leukoc Biol February 2011 89:259-267; doi:10.1189/jlb.0910486 ; <http://www.jleukbio.org/content/89/2/259.abstract>*



<http://www.scientificamerican.com/article.cfm?id=milk-of-life-dairy-cows-i>

## **Milk of Life: Dairy Cows Inoculated against Sepsis Could Help Malnourished Children** ***Researchers hope milk enriched with sepsis antibodies will be a safer and cheaper way to prevent illness and diarrhea in impoverished children***

**By Francie Diep | Monday, January 31, 2011 | 4**

Most people would probably prefer if traces of dairy cows' vaccinations don't show up in their milk, but one research team is looking into deliberately adding antibodies to milk as a way to help malnourished children in developing countries.

Seven years ago Alan Cross, a professor at the University of Maryland School of Medicine, published the results of a successful phase I clinical trial of a vaccine against sepsis he had developed. His next step, however, is to vaccinate dairy cows, not people. The cows will then produce an antibody-rich colostrum - the first milk mammals make after giving birth that transfers immunity to newborn animals - which organizations can give to malnourished children as a nutritional supplement.

Malnutrition causes the interior walls of the intestines to break down, allowing bacteria to move from the gut into the bloodstream, which leads to sepsis and a weakened immune system. For a child who has been malnourished for awhile, starting back on food is often insufficient to prevent illness and diarrhea, says Zeil Rosenberg, CEO of Bali Biosciences, LLC. The company has a license agreement with the University of Maryland, Baltimore, to produce the sepsis antibody colostrum. Rosenberg hopes that the milk, used along with food aid, will help break the "viscous cycle of malnutrition." In the past Rosenberg worked with Indonesia's Ministry of Health in Jakarta as a U.S. Agency for International Development advisor.

Once a child takes the colostrum, sepsis antibodies should enter his or her digestive system where they can bind to the toxins produced by sepsis-causing gram-negative bacteria such as *Escherichia coli*, Rosenberg says. The antibody-neutralized toxins might then leave the body via the feces, although researchers are not yet sure exactly how the colostrum will promote such evacuation.

Cross and Rosenberg also hope the antibody-rich milk will help trauma and burn patients, who are especially vulnerable to sepsis, but the first target audience for their product are malnourished children.

"It's an absolutely fascinating idea and completely original," says William Schaffner, a physician who researches infectious diseases at Vanderbilt University School of Medicine. Charles Arntzen, an Arizona State University School of Life Sciences biologist who studies vaccine development, says the idea sounds feasible as a way to block the onset of blood infection from the gut.

The colostrum should cost far less than conventional vaccine shots or intravenous treatment, making it less of a financial burden for developing nations. Rosenberg couldn't guess how much the final product might cost, but Arntzen notes that dairy cows make great quantities of colostrum, and immunizing cows is a common and inexpensive procedure.

Experts also expect the treatment to be very safe. Bali Biosciences will remove some of the lactose in the colostrum to make it more digestible for people who are lactose-intolerant, says Rosenberg. "As far as I can tell, they're not going to have any safety issues," Schaffner says. "This is like drinking [regular] cow's milk." The expected safety of the colostrum will help keep its test costs down.

Bali Biosciences continues to seek an organization to help distribute their product if it works, Cross says. Meanwhile, he'll be immunizing pregnant cows and testing their colostrum for the antibodies he's interested in. If the antibodies show up, he'll test the milk in animal models. He received a yearlong Maryland Proof of Concept Alliance grant last week to run his experiments.

In spite of billions of dollars spent in food aid, more than three million children die of malnutrition every year, according to the World Health Organization. Part of that mortality comes from infections that cross from the children's digestive systems into their blood, Rosenberg says. "We don't think there's one solution," he says, "but we think we can be part of a package of solutions."

<http://www.scientificamerican.com/article.cfm?id=did-vikings-navigate>

## **Did Vikings navigate by polarized light?**

***'Sunstone' crystals may have helped seafarers to find the Sun on cloudy days.***

**By Jo Marchant**

A Viking legend tells of a glowing "sunstone" that, when held up to the sky, revealed the position of the sun even on a cloudy day. It sounds like magic, but scientists measuring the properties of light in the sky say that polarizing crystals-which function in the same way as the mythical sunstone-could have helped ancient sailors to cross the northern Atlantic. A review of their evidence was published January 31 in *Philosophical Transactions of the Royal Society B*.

The Vikings, seafarers from Scandinavia who traveled widely and settled in swathes of Northern Europe, the British Isles and the northern Atlantic from around 750 to 1050 AD, were skilled navigators, able to cross thousands of kilometers of open sea between Norway, Iceland and Greenland. Perpetual daylight during the summer sailing season in the far north would have prevented them from using the stars as a guide to their positions, and the magnetic compass had yet to be introduced in Europe—in any case, it would have been of limited use so close to the North Pole.

But Viking legends, including an Icelandic saga centering on the hero Sigurd, hint that these sailors had another navigational aid at their disposal: a *sólarsteinn*, or sunstone.

The saga describes how, during cloudy, snowy weather, King Olaf consulted Sigurd on the location of the sun. To check Sigurd's answer, Olaf "grabbed a sunstone, looked at the sky and saw from where the light came, from which he guessed the position of the invisible sun." In 1967, Thorkild Ramskou, a Danish archaeologist, suggested that this stone could have been a polarizing crystal such as Icelandic spar, a transparent form of calcite, which is common in Scandinavia.

Light consists of electromagnetic waves that oscillate perpendicular to the direction of the light's travel. When the oscillations all point in the same direction, the light is polarized. A polarizing crystal such as calcite allows only light polarized in certain directions to pass through it, and can appear bright or dark depending on how it is oriented with respect to the light.

### **Centered on the light**

Scattering by air molecules in the atmosphere causes sunlight to become polarized, with the line of polarization tangential to circles centered on the sun. So Ramskou argued that by holding a crystal such as calcite up to the sky and rotating it to check the direction of polarization of the light passing through it, the Vikings could have deduced the position of the sun, even when it was hidden behind clouds or fog, or was just beneath the horizon.

Historians have debated the possibility ever since, with some arguing that the technique would have been pointless, because it would only work if the crystal was pointed at patches of clear sky, and in such conditions it would be possible to estimate the position of the sun with the naked eye, for example from the bright lining of cloud tops.

Gábor Horváth, an optics researcher at Eötvös University in Budapest, and Susanne Åkesson, a migration ecologist from Lund University, Sweden, have been testing these assumptions since 2005. The special issue of *Philosophical Transactions of the Royal Society B* in which their review appears is dedicated to biological research on polarized light.

In one study, the researchers took photographs of partly cloudy or twilight skies in northern Finland through a 180-degree fisheye lens, and asked test subjects to estimate the position of the sun. Errors of up to 99 degrees led the researchers to conclude that the Vikings could not have relied on naked-eye guesses of the sun's position.

To check whether sunstones would work better, in 2005 they measured the polarization pattern of the entire sky under a range of weather conditions during a crossing of the Arctic Ocean on the Swedish icebreaker *Oden*.

### **Through the clouds**

The researchers were surprised to find that in foggy or totally overcast conditions the pattern of light polarization was similar to that of clear skies. The polarization was not as strong, but Åkesson believes that it could still have provided Viking navigators with useful information. "I tried such a crystal on a rainy overcast day in Sweden," she says. "The light pattern varied depending on the orientation of the stone."

She and Horváth are now planning further experiments to determine whether volunteers can accurately work out the sun's position using crystals in various weather conditions.

Sean McGrail, who studied ancient seafaring at the University of Oxford, UK, before retiring, says that the studies are interesting but there is no real evidence to indicate that the Vikings actually used such crystals. "You can show how they could be used, but that isn't proof," he says. "People were navigating long before this without any instruments."

Surviving written records indicate that Viking and early medieval sailors crossed the north Atlantic using the sun's position on clear days as a guide, in combination with the positions of coastlines, flight patterns of birds, migration paths of whales and distant clouds over islands, says Christian Keller, a specialist in North Atlantic archaeology at the University of Oslo. "You don't need to be a wizard," he says. "But you do need to combine a lot of different sorts of observations."

Keller says he is "totally open" to the idea that the Vikings also used sunstones, but is waiting for archaeological evidence. "If we find a shipwreck with a crystal on board, then I would be happy," he says.

## **The Enema of Your Enemy is Your Friend**

***Fecal transplants could be a cheap and effective treatment for gastrointestinal disorders.***

**By Emily P. Walker**

One day in 2008, Ruth, a Long Island teacher, walked into her doctor's office with a container of a relative's feces, lay down, and had her doctor pump the stool inside her. Ruth had been suffering for nearly two years with an intestinal infection called *Clostridium difficile*, which caused her to suffer from excruciating diarrhea. She had lost 20 pounds. Her hair was falling out. Friends asked if she had cancer.

Then she met Lawrence Brandt, a gastroenterologist in the Bronx who believed he had developed a procedure to cure people of recurrent *c. diff* infections: fecal transplant. Brandt has been inserting feces into his patients for a decade now and claims to be solving their problems nearly 100 percent of the time. If his method really works - and he's not the only doctor who believes that it does - then we may have found a viable, if weird, solution to a serious problem. *C. diff* infects 250,000 Americans each year and killed more than 20,000 from 1999 to 2004. (Researchers estimate that 13 out of every 1,000 patients admitted to a hospital will pick up the bug.) Antibiotics will always be the first response to such infections, but when those fail, a fecal transplant could be the next step. For Ruth, at least, the procedure was a godsend. "I'm cured," she said. "Period. End of story. Cured."

Here's the basic idea. People suffering from the hardy *C. diff* bacteria are generally prescribed a powerful antibiotic. Problem is, the drugs don't just kill the invaders; they also wipe out much of the beneficial bacteria in the gut. With these "good" microorganisms out of the way, any *C. diff* stragglers have a much easier time regrouping for a second bout of illness. If there were some way to respawn the beneficial bacteria in the intestines, such re-infections could be warded off. Some people, like Ruth, turn to expensive probiotic supplements. (At one point she was spending \$350 on them every week.) But in certain cases, a patient who has lost nearly all of her good bacteria will find it nearly impossible to get them back. A fecal transplant seems to work as a sort of mega-probiotic, allowing doctors to repopulate a patient's intestines with the appropriate microorganisms by placing a robust sample directly into her gut.

Doctors recommend that the fecal donor be someone close to the patient - a family member, perhaps, or a spouse. Scientists reason that when people live in close quarters, they are exposed to similar bacteria - good and bad - and are likely to have had a similar set of bacteria living in their guts before anyone got sick.

The donor takes a stool softener the night before and then gives a full morning bowel movement to the recipient, who takes it to a doctor for screening. It's important to make sure that the sample doesn't contain any parasites or other pathogens, such as hepatitis, salmonella, or HIV. Once the transplant material has been cleared, the doctor mixes it with saline to make about a pint of liquid with the consistency of a milkshake. This is pumped into the patient's colon using a colonoscope or endoscope, or siphoned into the stomach via a nasogastric tube. (The latter method is considered more dangerous, since there's a chance feces will end up in the lungs. Colonoscopies carry their own risk of bowel perforation.)

And then there's the do-it-yourself crowd. All you need is a bottle of saline, a 2-quart enema bag, and one standard kitchen blender. Mike Silverman, a University of Toronto physician who wrote up a guide to homespun fecal transplants for the journal *Clinical Gastroenterology and Hepatology*, says it's entirely safe to do the procedure this way, provided that a doctor gets involved at some point to screen the donor sample. He felt he needed to draw up the instructions because administrators at his hospital wouldn't allow their doctors to perform a procedure that hasn't been validated in a large, peer-reviewed study.

It's true there's been no major clinical trial of fecal transplants, but the procedure appears in the medical literature at least as far back as 1958. That's when a Denver-based surgeon named Ben Eiseman performed four of the procedures to rid patients of a form of colitis thought to be caused by *C. diff*. His plan was to administer "normal feces into the colon of patients with the disease," so as to "re-establish the balance of nature." Three of his four patients were near death before the fecal enema. After, they recovered. This small experiment suggested a "simple yet rational therapeutic method," Eiseman and his colleagues wrote, that deserved careful evaluation.

Now we're beginning to see some more extensive studies. Mark Mellow, a gastroenterologist at INTEGRIS Health in Oklahoma City, recently presented a paper showing that 15 out of 16 *C. diff* patients whom he'd provided with a fecal transplant remained disease-free after five months. Several other papers presented at the meeting showed similar positive effects, and in every case, symptoms disappeared almost immediately after the transplant.

Still, the evidence supporting fecal transplant comprises just about 20 published case reports involving about 200 patients. Until a large-scale, randomized trial is published in a big-name medical journal, most doctors will

likely follow the example of the University of Toronto and hold off on performing the transplant. Indeed, relatively few gastroenterologists have even tried it. Colleen Kelly, a gastroenterologist at Women & Infants Hospital of Rhode Island, surveyed 72 gastroenterologists at a recent international medical meeting and found that only seven had performed the procedure. Nearly half said they'd be willing to perform a transplant on a sick patient, but the rest said they weren't ready yet. "I really think in another couple of years, it's going to be something that everyone's doing," said Kelly, who has performed the operation 22 times herself.

Infectious-disease experts are a little more tempered in their enthusiasm. According to Vincent Young of the University of Michigan, the data look promising but he wouldn't perform a fecal transplant himself because there are too many unknowns about what bad things might be lurking in a stool sample. William Schaffner, president of the National Foundation for Infectious Diseases, warned that the procedure is still in its early days and not yet ready for prime time. (The American College of Gastroenterology, for its part, has no official position on fecal transplants.)

But the true believers have even bigger plans. They hope fecal transplants might be used to treat other gut-related conditions, such as ulcerative colitis and even obesity. Some very overweight people, for example, are thought to have more of a certain type of bacteria in their intestines, which causes them extract extra calories from complex carbohydrates. With this in mind, researchers found that fat mice would lose weight if transplanted with feces from thin ones. Later, a team of Dutch researchers tried the same approach in humans: No one lost weight, but the fecal recipients did show a significant improvement in their ability to regulate insulin. (That study is under review and should be published in the next few months.)

For all its promise, it's unlikely fecal transplants will take off any time soon. Not because patients are grossed out by the procedure - in fact, doctors say that long-standing sufferers from *C. diff* are eager to have it done - but because there's so little funding for large-scale clinical trials. Drug or medical-device companies usually foot the bill for such research, but in the case of a natural, patent-free treatment like this, no company stands to turn a major profit. If anything, fecal transplants would end up costing the pharmaceutical companies money: A single pill of vancomycin - one of two antibiotics used to treat *C. diff* - costs about \$55, and the average dose is four pills daily over a two-week stretch. A glass of shit, on the other hand, costs very little. That doesn't mean we'll never get the much-needed data: Lawrence Brandt, the gastroenterologist in the Bronx, is applying for a grant with the National Institutes of Health for a small, double-blind, controlled study. He says he'll need about 40 patients, and he's hoping to get started right away.

<http://www.scientificamerican.com/article.cfm?id=south-carolina-scientist-works-to-g>

### **South Carolina scientist works to grow meat in lab**

***In a small laboratory on an upper floor of the basic science building at the Medical University of South Carolina, Vladimir Mironov, M.D., Ph.D., has been working for a decade to grow meat.***

**By Harriet McLeod**

CHARLESTON, South Carolina (Reuters) - In a small laboratory on an upper floor of the basic science building at the Medical University of South Carolina, Vladimir Mironov, M.D., Ph.D., has been working for a decade to grow meat. A developmental biologist and tissue engineer, Dr. Mironov, 56, is one of only a few scientists worldwide involved in bioengineering "cultured" meat. It's a product he believes could help solve future global food crises resulting from shrinking amounts of land available for growing meat the old-fashioned way ... on the hoof.

Growth of "in-vitro" or cultured meat is also under way in the Netherlands, Mironov told Reuters in an interview, but in the United States, it is science in search of funding and demand.

The new National Institute of Food and Agriculture, part of the U.S. Food and Drug Administration, won't fund it, the National Institutes of Health won't fund it, and the National Aeronautics and Space Administration funded it only briefly, Mironov said. "It's classic disruptive technology," Mironov said. "Bringing any new technology on the market, average, costs \$1 billion. We don't even have \$1 million." Director of the Advanced Tissue Biofabrication Center in the Department of Regenerative Medicine and Cell Biology at the medical university, Mironov now primarily conducts research on tissue engineering, or growing, of human organs.

"There's a yuck factor when people find out meat is grown in a lab. They don't like to associate technology with food," said Nicholas Genovese, 32, a visiting scholar in cancer cell biology working under a People for the Ethical Treatment of Animals three-year grant to run Dr. Mironov's meat-growing lab.

"But there are a lot of products that we eat today that are considered natural that are produced in a similar manner," Genovese said. "There's yogurt, which is cultured yeast. You have wine production and beer production. These were not produced in laboratories. Society has accepted these products."

If wine is produced in winery, beer in a brewery and bread in a bakery, where are you going to grow cultured meat? In a "carnery," if Mironov has his way. That is the name he has given future production facilities.

He envisions football field-sized buildings filled with large bioreactors, or bioreactors the size of a coffee machine in grocery stores, to manufacture what he calls "charlem" - "Charleston engineered meat."

"It will be functional, natural, designed food," Mironov said. "How do you want it to taste? You want a little bit of fat, you want pork, you want lamb? We design exactly what you want. We can design texture.

"I believe we can do it without genes. But there is no evidence that if you add genes the quality of food will somehow suffer. Genetically modified food is already normal practice and nobody dies."

Dr. Mironov has taken myoblasts - embryonic cells that develop into muscle tissue - from turkey and bathed them in a nutrient bath of bovine serum on a scaffold made of chitosan (a common polymer found in nature) to grow animal skeletal muscle tissue. But how do you get that juicy, meaty quality?

Genovese said scientists want to add fat. And adding a vascular system so that interior cells can receive oxygen will enable the growth of steak, say, instead of just thin strips of muscle tissue. Cultured meat could eventually become cheaper than what Genovese called the heavily subsidized production of farm meat, he said, and if the public accepts cultured meat, the future holds benefits.

"Thirty percent of the earth's land surface area is associated with producing animal protein on farms," Genovese said. "Animals require between 3 and 8 pounds of nutrient to make 1 pound of meat. It's fairly inefficient. Animals consume food and produce waste. Cultured meat doesn't have a digestive system.

"Further out, if we have interplanetary exploration, people will need to produce food in space and you can't take a cow with you. "We have to look to these ideas in order to progress. Otherwise, we stay static. I mean, 15 years ago who could have imagined the iPhone?" (Editing by Jerry Norton)

<http://www.scientificamerican.com/podcast/episode.cfm?id=moms-infection-helps-kids-skin-11-01-31>

### **Moms' Infection Helps Kids' Skin**

***The children of women with untreated worm infections while pregnant had fewer cases of eczema, lending further credence to the "hygiene hypothesis" that says that some immune challenges may have long-term benefits. [Listen to this Podcast](#)***

Cynthia Graber comments

Can we be too clean? According to what's called the hygiene hypothesis, yes. Without being challenged as kids, our immune systems don't flourish. Scientists think it could be part of the rise of allergies and asthma.

Now a new study supports the hygiene hypothesis: infants in Uganda had a lower chance of developing the skin allergy condition eczema if their moms had helminth worm infections while pregnant. The research is in the journal *Pediatric Allergy and Immunology*. [Harriet Mpairwe et al., "Anthelmintic treatment during pregnancy is associated with increased risk of infantile eczema: randomised-controlled trial results"]

A 2005 study showed that the kids of women treated for worm infections had more eczema. Twenty-five hundred pregnant women took part in this follow-up research. Some got one worm-killing drug. Others took a different drug. And a third group received a placebo. One drug nearly doubled the kids' risk of eczema. The other more than doubled the odds.

Helminth worm infections can give the mothers symptoms such as mild anemia or stomach pain and vomiting. Although many people have no symptoms at all. The scientists say more research is needed before they would recommend not treating worm infections. But the work lends additional support to the idea that hygiene may be a balancing act rather than a goal.

<http://www.newscientist.com/article/dn20050-haiti-polio-scare-may-be-rare-complication-of-cholera.html>

### **Haiti polio scare may be rare complication of cholera**

\* 16:41 31 January 2011 by Debora MacKenzie

***Finally, some good news for Haiti: after three months, the cholera epidemic is starting to subside. And fears that polio had broken out may have been premature.***

A handful of people with polio-like symptoms may instead have had a previously unreported complication of cholera treatment. Several people in the north of the country were reported to have developed paralysis late last year after being successfully treated for cholera. "Polio was one of the first possibilities looked into because of the public health implications," the World Health Organization's office for the Americas stated last week.

That is an understatement. Like cholera, polio – which causes paralysis – is carried in water and human faeces, and an outbreak would wreak havoc in Haiti, where sanitation is poor and diarrhoea and extreme poverty would help spread the virus. It would also threaten the worldwide eradication effort.

### **Reverted and dangerous**

Polio was declared gone from the Americas in 1994, but in 2000 there were cases in Haiti and the neighbouring Dominican Republic. They were caused by the weakened, live virus in the polio vaccine, which had reverted to a dangerous form and begun circulating, as some health experts had warned it might.

But wild polio virus, still circulating in Africa and Asia, is a bigger threat – so 200,000 Haitian children have been vaccinated against the disease since the earthquake in the country in January 2010. Reports of paralysis woke fears that the vaccine virus had escaped again. Last week, however, the WHO announced that on investigation, only four cases really looked like polio, and of those people three died – too high a death rate for polio. Pending results of tests for polio virus, it says it is "likely to rule out polio".

### **Salt in the blood**

So what is it? The people developed paralysis one to three days after finishing cholera treatment. Niklas Danielsson of the European Centre for Disease Control and Prevention in Stockholm, Sweden, says this suggests osmotic demyelination syndrome (ODS). ODS afflicts people whose blood salts are too low for two days or more, then return to normal too quickly. It results in destruction of the myelin sheaths around nerve cells, causing symptoms similar to the reports from Haiti.

"This has never been reported in cholera before, but I think it is a real possibility," says Mitchell Rosner, an ODS expert at the University of Virginia in Charlottesville.

### **Rare imbalance**

If the concentration of sodium in blood falls, more water flows into cells by osmosis, causing them to swell. Nerve cells in the brain can be damaged if the glial cells that form the myelin sheaths around them swell.

If osmotic pressure persists, glial cells protect against this damage by reducing their own internal osmotic pressure so that they don't swell. However, if blood salt returns to normal quickly, the glial cells cannot adapt back fast enough. The normal osmotic pressure shrinks the cells, destroying them, says Rosner.

Both cholera and rehydration treatment cause low blood sodium which can last for several days, says Danielsson. ODS could be triggered when the blood returns to normal after treatment stops. An MRI scan of neural tissue could settle it, says Rosner, as ODS causes typical patterns of damage. It's a devastating diagnosis for the people involved – but the good news for Haiti is that, unlike polio, ODS isn't infectious.

<http://www.scientificamerican.com/article.cfm?id=controversy-french-classrooms-modifying-bacteria>

## **Controversy Erupts in French Classrooms over Permitting Teens to Genetically Modify Bacteria**

***Opponents fear that experiments will 'trivialize' genetic modification.***

**By Barbara Casassus**

A row has broken out in France over whether 15- and 16-year-olds should be allowed to create transgenic *Escherichia coli* bacteria in the classroom. Practical experiments in which students learn how to use plasmids to alter the DNA of the bacteria have been under way for 17 and 18-year-olds in the final year of the scientific baccalaureate at schools across France for the past decade. But this year teachers have for the first time been offered the option of teaching the experiments to younger students.

The Committee for Research & Independent Information on Genetic Engineering (CRIIGEN) in Caen, France, which lobbies for stricter controls over genetic engineering, is particularly upset because in the experiments the students modify the bacteria to become resistant to the antibiotic ampicillin.

Gilles-Eric S eralini, president of the organization's scientific committee, says that CRIIGEN is in favor of genetic engineering, as long as it is properly controlled. But the necessary restrictions are not currently in place, he says. CRIIGEN "will urge the education ministry to impose a moratorium until a full debate on the question is organized", says S eralini. "We believe such material should not be manipulated by students before they reach university."

He warns against trivialization of a sensitive subject, contamination risks and possible violation of European directives on the manipulation of genetically modified organisms in confined spaces. "I am also concerned that practical classes erode the time spent imparting knowledge of biology," he adds.

Luc Chatel, France's education minister, today unveiled a plan to encourage more students to opt for science and technology subjects at university by improving teaching in schools, but he told *Nature* that increasing the amount of compulsory practical work is not part of the scheme. Schools can choose how much time they devote to experiments, as long as students are prepared for the hands-on work that makes up 20% of marks in the scientific baccalaureate exam at 18.

### **Nothing to worry about**

The French Association of Biology and Geology Teachers (APBG) in Lyons, which sells kits of *E. coli* with instructions for genetic modification to teachers, dismisses CRIIGEN's concerns.

These practical experiments have been part of the biology option for 17-18-year-old science baccalaureate students for ten years, and are not compulsory for younger pupils, says Serge Lacassie, president of the APBG, who teaches biology and geology at the Lyc e Berthollet in Annecy.

Only a few teachers include hands-on transgenesis in their courses for 15 and 16-year-olds, and Lacassie is not among them. He says that this is because of time constraints, although he acknowledges that students in their mid-teens are "perhaps not aware of the danger of manipulating such material". The biggest risk is that the bacteria could escape into the environment, so "we teach students how to take the necessary precautions to ensure this doesn't happen", he says. In addition, "the bacteria are not pathogenic and are destroyed with bleach when experiments are over".

### **Practical advantage**

Lacassie stresses that practical classes teach students how to work in sterile conditions without damaging the environment. "We need to teach science according to the realities of today-DNA is a universal language and it is useful to experience how a gene can be transferred from one organism to another. Our aim is to give students the elements to reflect about biotechnology in general," he says.

The E. coli kits are supplied to the APBG by the DNA School Association in Nîmes. "We launched the product in 2002, and sell about 50 a year," says Jean-Christophe Lallement, the association's director. "That is fewer than at first. We have never had a problem with them, but now some biology teachers prefer to buy our DNA-fingerprinting kits instead," he says.

Valérie Sipahimalani, national secretary in charge of biology and geology for the National Union of Secondary Teachers, part of the Unitary Union Federation in Paris, has no objection to practical transgenesis classes, provided that the safety rules are respected. "It is up to teachers to decide," she says.

But she does not run the practical lessons at her school in Paris, because it is not a priority and because the equipment is too expensive. "Personally, I don't believe in teaching manipulation for manipulation's sake," she says. "More importantly, DNA takes a lot of time to explain-it is very complicated for secondary school-students to understand."

<http://www.physorg.com/news/2011-01-african-americans-survival.html>

### **Study: African-Americans have better stroke survival rates**

***A study published today shows that African Americans have a better survival rate compared to whites after being hospitalized for a stroke.***

This conclusion contradicts prevailing wisdom and is one piece in a growing body of evidence that points to the important role that patients – and the decision they and their families make in terms of treatment – may play on mortality rates.

The study found that - after adjusting data for variables such as age, socioeconomic status, and risk factors - that African Americans who were hospitalized for acute ischemic stroke had a significantly lower mortality rate than whites. The survival advantage was most pronounced early after the stroke but persisted for up to one year. The study also found that African Americans were also more likely during their hospitalization to have received more aggressive treatment measures, such as kidney dialysis, a tracheostomy, or cardiopulmonary resuscitation. They were also less likely to use hospice care. These results were published today in the *Annals of Internal Medicine*.

"These results fly in the face of conventional wisdom that says that black patients with strokes have worse outcomes," said University of Rochester Medical Center (URMC) neurologist Robert Holloway, M.D., M.P.H. a co-author of the study. "Even though we do not know the exact reasons for these differences, these data highlight the potential importance of treatment intensity, and the expression of patient preference for different treatments on survival and mortality. This is not such a far-fetched idea for physicians who take care of a lot of stroke patients."

"We know that African Americans have a higher prevalence of stroke and higher risk factors for stroke," said Ying Xian, M.D., Ph.D., a former graduate student in Health Services Research and Policy with URMC Department of Community and Preventive Medicine and now a fellow with the Duke Clinical Research Institute and co-author of the study. "But this data shows that African Americans have lower mortality rates than whites. It also shows that African Americans are more likely to be treated aggressively and we suspect that this may have an impact on their mortality outcomes."

The study used data from the New York State Statewide Planning and Research Cooperative System, a reporting system that collects detailed information on every hospital and emergency department admission in the state. They compiled information for all non-Hispanic blacks and non-Hispanic whites age 18 and older who were admitted to a hospital with a diagnosis of acute ischemic stroke in 2005 and 2006.

The researchers used a novel statistical approach to minimize the difference between two pools of black and white patients in terms of demographic profiles, co-morbidities, and the type of hospital where they received their care. They then looked at mortality rates for several incremental periods beginning at 7 days and up to a year after the stroke and what life-sustaining interventions the patients received during their hospitalization.

The authors found that over the course of the year African American patients had a statistically lower rate of mortality and at the same time were more likely to receive aggressive life-sustaining treatments.

While the data used for the study does not illustrate the role of patient preference – either expressed intent or in the form of do not resuscitate orders, health care proxies, or living wills – or the decisions made by family member on their behalf, the authors believe the evidence indicates that there might be a link between the treatment decisions made by patients and their families when seriously ill with stroke and survival rates.

"Although we don't show any causal relationship, the association of lower risk of death and increased use of life-sustaining interventions is actually very consistent with the idea that preference sensitive end-of-life care may have an important impact on short-term mortality," said Holloway. "We were unable to measure health or quality of life in those patients who survived, which is a critically important question. We also need much more research on ways to measure the quality of the decision process itself to make sure that the treatments patients receive are consistent with their underlying values and preferences."

"Even though people who receive aggressive life-sustaining care have lower mortality it does not mean they have better quality of care or quality of life," said Xian. "Mortality is important measure but not only measure."

*Provided by University of Rochester Medical Center*

[http://www.eurekalert.org/pub\\_releases/2011-02/epfd-anm020111.php](http://www.eurekalert.org/pub_releases/2011-02/epfd-anm020111.php)

### **A new model for studying Parkinson's**

#### ***Swiss researchers develop new, working mammalian model to combat genetic causes of the disease***

Evidence is steadily mounting that genetic factors play an important role in many cases of Parkinson's disease (PD). In a study published February 2, 2011, online in the Journal of Neuroscience, researchers from the Ecole Polytechnique Fédérale de Lausanne (EPFL) in Switzerland report a new mammalian model for studying a specific gene mutation commonly found in PD sufferers, opening the door to new drugs to fight the malady.

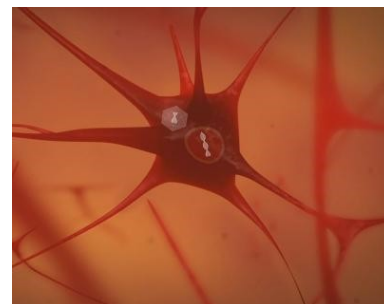
"This is a great step forward toward a more comprehensive understanding of how the disease works, and how it can be diagnosed and treated," explains neuroscientist and EPFL President Patrick Aebischer, lead author of the study.



***This is a cervical slice showing the healthy left-hand side of the brain and the damaged, Parkinson's disease side with lesions provoked by the LRRK2 gene mutation. EPFL***

PD is a common neurodegenerative disease that greatly reduces quality of life and costs the United States around 23 billion dollars a year. Until now, researchers have encountered difficulty in reproducing PD pathology in animals because of an incomplete understanding of the disease.

Recently, a mutation of the gene coding for LRRK2, a large enzyme in the brain, has emerged as the most prevalent genetic cause of PD (genetics are implicated in about 10 percent of all PD cases). When the enzyme is mutated, it becomes hyperactive, causing the death of vulnerable neurons and leading to a reduction in levels of the brain neurotransmitter dopamine. This decrease in dopamine eventually triggers the symptoms characteristic of Parkinson's, such as tremors, instability, impaired movement, and later stage dementia.



***A vector is introduced into the healthy brain cell and transmits the mutated gene. EPFL***

Now, with funding from the Michael J. Fox Foundation for Parkinson's Research, Aebischer and his team in the Neurodegenerative Studies Laboratory at EPFL, have successfully introduced mutant LRRK2 enzyme into one hemisphere of a rat brain, resulting in the same PD manifestations that occur in humans in one side of the rodent's body. To do this, the researchers spent two years producing and optimizing a viral vector to deliver mutated, LRRK2 coding DNA into the rat brain. LRRK2 is a large and complicated enzyme and designing a vector capable of transporting its extremely long genetic code was no small feat.

The new animal model developed by EPFL is sure to benefit future Parkinson's research. The fact that LRRK2 is an enzyme - a catalyzing protein involved in chemical reactions - makes it drug accessible and therefore of specific interest to researchers looking for neuroprotective strategies, or pharmaceutical treatments that halt or slow disease progression by protecting vulnerable neurons. Armed with the LRRK2 model, new pharmaceuticals that inhibit the hyper-activity of the enzyme could one day prevent the destructive chain of events that leads to neurodegeneration and devastation in many with PD.



[http://www.eurekalert.org/pub\\_releases/2011-02/haog-apc020111.php](http://www.eurekalert.org/pub_releases/2011-02/haog-apc020111.php)

### **A possible cause of Parkinson's disease discovered**

**"Nucleolus", or small nucleus, is the term coined by early biologists for the tiny structure within the nucleus which they saw under the microscope. In this structure within the nucleus, RNA molecules and proteins are assembled to form ribosomes, the true protein factories of cells.**

Defective nucleoli have been implicated in several rare hereditary diseases, most recently also in neurodegenerative disorders such as Alzheimer's and Huntington's disease. Despite intense research efforts around the world, the molecular causes of Parkinson's disease are still unclear. Under the leadership of Dr. Rosanna Parlato, scientists from the departments of Professor Dr. Guenther Schuetz and Professor Dr. Ingrid Grummt at DKFZ have investigated whether the demise of nucleoli also plays a role in this disease, which is also known as "shaking palsy".

The investigators studied dopamine-producing neurons in the brain of Parkinson's disease patients under the microscope. When Parkinson's disease occurs, this type of cells malfunctions and dies, causing the characteristic palsy symptoms. Indeed, the majority of nucleoli in these cells were found to be defective.

This discovery caused the group to investigate whether disrupted nucleoli may really cause Parkinson's-like symptoms or whether this was only an incidental finding. To this end, they modified the DNA of mice in such a way that the dopamine-producing cells of the experimental animals could only form defective nucleoli. These mice showed symptoms resembling Parkinson's disease, such as characteristically impaired movements. In addition, the dopamine-producing neurons in their brain died prematurely.

In order to find out why these symptoms occur, the researchers took a closer look at all functions of the genetically modified cells. And they found an important change: The activity of the mTOR enzyme, a key regulator of intracellular signaling pathways, was reduced in the genetically modified cells. As a result of reduced mTOR activity, the function of mitochondria, the cellular power plants, is disrupted. This functional disruption causes oxidative stress within the cell; highly reactive oxygen compounds accumulate and cause damage to a multitude of molecules in the cell.

"Defective nucleoli apparently cause oxidative stress in cells. This can lead to massive cell damage and may be a key prerequisite for the typical nerve damage of Parkinson's disease," says Dr. Rosanna Parlato. "The dopamine-producing neurons are particularly sensitive to oxidative stress." However, the scientists are not sure whether the damage in the nucleoli is really the sole cause of this neurodegeneration. "In any case, the nucleolus functions as a stress sensor showing us that a cell is in danger."

*Claus Rieker, David Engblom, Grzegorz Kreiner, Andrii Domanskyi, Andreas Schober, Stefanie Stotz, Manuela Neumann, Xuejun Yuan, Ingrid Grummt, Günther Schütz and Rosanna Parlato: Nucleolar Disruption in Dopaminergic Neurons Leads to Oxidative Damage and Parkinsonism through Repression of Mammalian Target of Rapamycin Signaling. The Journal of Neuroscience, January 12, 2011, 31(2):453–460, DOI:10.1523/JNEUROSCI.0590-10.2011*

[http://www.eurekalert.org/pub\\_releases/2011-02/vt-soa012711.php](http://www.eurekalert.org/pub_releases/2011-02/vt-soa012711.php)

### **Size of airborne flu virus impacts risk, Virginia Tech researchers say**

**A parent's wise advice to never go to a hospital unless you want to get sick may be gaining support from scientific studies on a specific airborne virus.**

The results of a Virginia Tech study by environmental engineers and a virologist on the risk of airborne infection in public places from concentrations of influenza A viruses is appearing today in the on-line, Feb. 2 issue of the United Kingdom's Journal of the Royal Society Interface.

Linsey Marr, associate professor of civil and environmental engineering at Virginia Tech, <http://www.cee.vt.edu/people/lmarr.html> and her colleagues, Wan Yang, of Blacksburg, Va., one of her graduate students, and Elankumaran Subbiah, a virologist in the biomedical sciences and pathobiology department of the Virginia-Maryland Regional College of Veterinary Medicine, <http://www.vetmed.vt.edu/org/dbsp/faculty/subbiah.asp> conducted their research in a health center, a daycare facility, and onboard airplanes.

"The relative importance of the airborne route in influenza transmission - in which tiny respiratory droplets from infected individuals are inhaled by others - is not known," Marr, who received a National Science Foundation CAREER Award to pinpoint sources of unhealthy air pollutants, said.

What is known is that influenza A viruses are "transmitted through direct contact, indirect contact, large respiratory droplets, and aerosols that are left behind by the evaporation of larger droplets," they reported in the journal. "The aerosol transmission route is particularly controversial since there is scant proof of infection mediated by virus-laden aerosols, partly due to the difficulties in studies involving human subjects and partly due to the challenges in detecting influenza A viruses in ambient air."

What happens is an infected person might cough or sneeze or just be engaged in conversation, and release the viruses into the air. However, these aerosols are quickly diluted to very low concentrations by the surrounding air.

Marr said, "Few studies have measured actual concentrations of influenza A viruses in air and determined the size of influenza-laden particles. Size is important because it determines how long the particles will remain suspended in the air before being removed due to the forces of gravity or other processes."

To conduct their studies, the Virginia Tech researchers collected samples from a waiting room of a health care center, two toddlers' rooms and one babies' area of a daycare center, as well as three cross-country flights between Roanoke, Va., and San Francisco, Ca. They collected 16 samples between Dec. 10, 2009 and Apr. 22, 2010.

"Half of the samples were confirmed to contain aerosolized influenza A viruses," Marr said. "In the others, it is possible that no infected individuals were present." Marr added, "The average concentration was 16,000 viruses per cubic meter of air, and the majority of the viruses were associated with fine particles, less than 2.5 micrometers, which can remain suspended for hours. Given these concentrations, the amount of viruses a person would inhale over one hour would be adequate to induce infection."

Subbiah indicated that most studies of airborne transmission of influenza viruses in animals examined the ability of infected animals to transmit the infection to susceptible in-contact animals. How the ambient environment affects the virus after release from the infected host until it reaches the recipient host is relatively unknown. Results of the study show that under defined conditions of humidity and temperature, viruses may remain suspended in air.

Incorporating the concentrations of influenza A viruses and breathing rates, Marr and her colleagues estimated the inhalation dose incurred by someone in the same room and concluded that it was sufficient to induce infection. "As a whole," the three authors concluded in the *Journal of the Royal Society Interface*, "our results provide quantitative support for the possibility of airborne transmission of influenza in indoor environments."

[http://www.eurekalert.org/pub\\_releases/2011-02/mc-nsa020111.php](http://www.eurekalert.org/pub_releases/2011-02/mc-nsa020111.php)

### **New study alters long-held beliefs about shingles**

**ROCHESTER, Minn. - *For decades, medical wisdom about shingles has been that it's a once-in-a-lifetime experience.***

The commonly-held belief is that patients are protected from a recurrence of the herpes zoster virus, which causes shingles, after one episode. But according to a study published in the February issue of *Mayo Clinic Proceedings*, recurrences of shingles may be significantly more common than doctors have suspected.

"It's been thought that recurrences were limited to people with compromised immune systems, for instance from chemotherapy or bloodborne malignancies, but this is not the case," says lead author Barbara Yawn, M.D., director of research at Olmsted Medical Center in Rochester. "Recurrence was prevalent in the immunocompetent population. We were very surprised by the results."

The research team examined medical records, dating from 1996 to 2001, of nearly 1,700 patients over age 22 who had a documented episode of shingles. The condition causes a specific type of skin rash and severe pain. They then searched area medical records to determine whether those patients had been treated for a second episode at any point, following them up to 12 years (the average follow-up was eight years). The data showed the recurrence rate was over 5 percent, the same rate an age-matched cohort would be expected to experience a first case of shingles. Some patients had experienced as many as three recurrences. "And that's only within eight years," Dr. Yawn notes. "As you continue to follow these patients throughout their lives, it's likely the recurrence rate will be much higher than 5 percent."

The study found that women, who are more likely than men to have shingles, also were more likely to experience a recurrence of the disease. Although the team had suspected that recurrence rates would be higher in older patients, age did not appear to make individuals more susceptible to another round of the disease. Instead, researchers found the most striking determinant for recurrence was patients' pain during the initial episode. Those who had experienced pain lasting more than 30 days after the initial onset of shingles were more likely to face a recurrence, particularly in the first three to four years after the initial episode. This, too, surprised the research team. "We'd thought that suffering a worse case would possibly give patients more resistance to a second occurrence, but our data presented the exact opposite," says Dr. Yawn.

The results suggest that the herpes zoster vaccine, which is known to reduce first-time occurrences of shingles by 50 percent, may help patients avoid a second episode. "Until now, we haven't been able to tell patients their risks of getting zoster a second time," Dr. Yawn says. "This study offers another piece of information for patients and doctors who are discussing the likelihood of recurrence and considering a prevention strategy."

## **Targeted particle fools brain's guardian to reach tumors**

### ***By impersonating iron, binding agent glides through the blood-brain barrier***

HOUSTON - A targeted delivery combination selectively crosses the tight barrier that protects the brain from the bloodstream to home in on and bind to brain tumors, a research team led by scientists from The University of Texas MD Anderson Cancer Center reported in the January issue of the Journal of Clinical Investigation.

In experiments with mice, the researchers demonstrated that the targeted particles guide payloads to image tumors, treat tumors, or can potentially do both to monitor treatment as it occurs. Their findings open a new research avenue for detecting and treating brain tumors in human patients.

"We've identified an iron-mimic peptide that can hitch a ride on a protein complex that transports iron across the blood-brain barrier," said co-senior author Wadih Arap, M.D., Ph.D., professor in the David H. Koch Center at MD Anderson. "Employing the iron transport system selectively opens the blood-brain barrier for tumor imaging and treatment while keeping it otherwise intact to play its protective role."

The barrier thwarts drug delivery because its tight layering of blood vessel cells and certain types of brain cells forms a nearly impenetrable wall against most blood-borne compounds, which can harm the brain. The iron-transporting transferrin protein and receptor complex is a potential path to treatment, the authors noted, because its receptor gene is the most overexpressed in human glioblastomas.

Glioblastomas are the most common form of primary brain tumor among adults and are one of the most lethal cancers - patients have a median survival rate of one year. They resist radiation and chemotherapy and often invade areas of the brain where full surgical removal is impossible.

### **Peptide + viral particle = targeting**

Arap and Renata Pasqualini, Ph.D., professor in the Koch Center and co-senior author on the paper, developed the screening, targeting and delivery processes used in the project. The combination consists of a viral particle called phage packaged with a bit of protein, or peptide, which acts as a ligand, binding to the target.

"This particular delivery system can evolve on many fronts, but we think imaging will probably be the first priority," Pasqualini said. "Brain tumors invade the brain in unpredictable ways, making surgery and targeted therapy a challenge. Ligand-directed imaging based on this technology might improve existing treatment strategies."

The team is working toward phase I human clinical trials, but required preclinical steps will take at least two years. "Our priority is the rapid translation of our approach into clinical applications, an effort that will greatly benefit from the collaborative, multidisciplinary nature of this project," said co-first author Fernanda Staquicini, Ph.D., a postdoctoral fellow in the Arap-Pasqualini lab.

The researchers screened potential binding agents to brain blood vessel cells in mice from a library of small peptides attached to viral particles. Analysis narrowed 30 candidates out of hundreds screened down to one peptide: CRTIGPSVC, a portion of the transferrin protein.

The iron-binding protein transferrin has two conformations, one when it's iron-free (open) and another when it contains iron (closed). Experiments showed that CRTIGPSVC connects with the open form, converting the protein to a state similar to the closed form, as if it were carrying iron. The closed form binds to transferrin receptors, which exist in abundance in glioblastoma.

### **Peptide phage selectively sticks with tumors**

The CRTIGPSVC peptide phage was given to mice with human-derived malignant glioma. An hour later, the tumors harbored high levels of the peptide phage, which appeared at only background levels in normal tissue.

Immunostaining showed the peptide phage gathered in both the tumor's blood vessels and tumor tissue, indicating that it passed from the blood vessels to tumor cells.

### **Guided payloads shrink and image tumors**

The CRTIGPSVC peptide was then connected to a viral delivery system loaded with a gene from the Herpes' simplex virus known as HSVtk. It serves as a reporter gene for molecular imaging with PET scans and causes cells to kill themselves when given with the drug ganciclovir.

\* Mice treated with the CRTIGPSVC-targeted versions loaded with the HSVtk gene had tumors that were typically half the size of those in mice treated with the untargeted delivery system when both groups were treated with ganciclovir.

\* Blood vessel and glioma cells forced to commit suicide (apoptosis) were found throughout the tumors of mice treated with the peptide-targeted delivery system. Cell suicide did not occur above background levels in normal brain tissue.

\* PET/CT scans showed widespread targeting of tumor tissue with little or no signal in normal tissue.

The team analyzed expression of the transferrin receptor in 165 samples of human tumors. A strong or moderate presence of the receptor was found on 85 percent of glioblastoma samples, indicating that the receptor might be a suitable target for human use.

### **Beyond cancer: Genetic defects, neurodegenerative diseases**

Peptide-guided delivery of drugs or imaging agents could apply to other diseases of the central nervous system, said co-author Richard Sidman, M.D., emeritus professor of neuropathology at Harvard Medical School and the Department of Neurology at Beth Deaconess Medical Center.

"One important set of diseases to test will be lysosomal storage diseases, mostly lethal in childhood or adolescence, in each of which a different crucial brain enzyme is markedly reduced or absent because of a defect in the corresponding gene," Sidman said. "These diseases can be treated by provision to the brain of 25 percent or less of the missing enzyme. Therefore, the prospect merits testing as to whether delivery of even modest amounts of the normal version of the pertinent gene across the blood-brain barrier would be therapeutically effective."

Prospects for radiologically diagnosing and treating strokes, traumatic injury and neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's diseases, also are worth pursuing, Sidman noted.

An accompanying commentary in JCI notes the flexibility and utility of the researchers' plan of attack. "We can look forward to future applications of this approach for the discovery of new druggable targets and the identification of cell surface molecules that may be important in many types of cancer as well as other diseases," concluded co-authors David Nathanson, M.D., and Paul Mischel, M.D., of the David Geffen School of Medicine at UCLA.

*The research project was funded by grants from the National Institutes of Health, the National Cancer Institute, the U.S. Department of Defense and MD Anderson's Center for Targeted Therapy; also by awards from the Gillson-Longenbaugh Foundation, AngelWorks, the Marcus Foundation, and the National Foundation for Cancer Research, the Harry S. and Isabel C. Cameron Foundation and the Schissler Foundation. Other authors are co-first authors Michael Ozawa, Ph.D., and Catherine Moya, Ph.D., both of whose doctoral dissertations emerged from this project, Wouter Driessen, Ph.D., and E. Magda Barbu, Ph.D., of MD Anderson's Koch Center; Hiroyuki Nishimori, M.D., Ph.D., Frank B. Furnari, Ph.D., and Webster K. Cavenee, Ph.D., of the Ludwig Institute for Cancer Research, University of California San Diego; Suren Soghomonyan, Ph.D., Leo G. Flores 2nd, M.D., Ph.D., Vincenzo Paolillo, Ph.D., Mian M. Alauddin, Ph.D., and Juri G. Gelovani, M.D., Ph.D., of MD Anderson's Department of Experimental Imaging; Xiaowen Liang and Magnus Höök, Ph.D., of Texas A&M University Health Science Center, Houston; James P. Basilion, Ph.D., of the Center for Molecular Imaging Research and National Foundation for Cancer Research (NFCR) Center for Molecular Analysis and Imaging, Massachusetts General Hospital; Oliver Bogler, Ph.D., and Frederick Lang Jr., M.D., of MD Anderson's Department of Neurosurgery; and Kenneth Aldape, M.D., and Gregory Fuller, M.D., Ph.D., of MD Anderson's Department of Pathology; The University of Texas, Arap and Pasqualini have an equity interest in Mercator Therapeutics, which is subject to restrictions under university policy. MD Anderson manages the terms of these arrangements in accordance with its conflict of interest policies.*

<http://www.physorg.com/news/2011-02-safety-checklist-yields-percent-hospital.html>

### **Safety checklist use yields 10 percent drop in hospital deaths**

**A Johns Hopkins-led safety checklist program that virtually eliminated bloodstream infections in hospital intensive-care units throughout Michigan appears to have also reduced deaths by 10 percent, a new study suggests.**

Although prior research showed a major reduction in central-line related bloodstream infections at hospitals using the checklist, the new study is the first to show its use directly lowered mortality.

"We knew that when we applied safety science principles to the delivery of health care, we would dramatically reduce infections in intensive care units, and now we know we are also saving lives," says Peter J. Pronovost, M.D., Ph.D., a professor of anesthesiology and critical care medicine at the Johns Hopkins University School of Medicine and leader of the study published in BMJ, the British medical journal. "Thousands of people are believed to have survived because of this effort to reduce bloodstream infections."

Pronovost's previous research has shown that coupling a cockpit-style, infection-control checklist he developed with a work environment that encourages nurses to speak up if safety rules aren't followed reduced ICU central-line bloodstream infections to nearly zero at The Johns Hopkins Hospital and at hospitals throughout the states of Michigan and Rhode Island. Experts say an estimated 80,000 patients a year with central lines get infected, some 31,000 die - nearly as many as die from breast cancer annually - and the cost of treating them may be as high as \$3 billion nationally.

For the new study, Pronovost and his team, using Medicare claims data, studied hospital mortality of patients admitted to ICUs in Michigan before, during and after what is known as the Keystone ICU Project, which features the checklist. They compared the Michigan information to similar data from 11 surrounding states. While data from both Michigan and the other states showed a reduction in hospital deaths of elderly patients

admitted to ICUs over the five-year period from October 2001 to December 2006, the patients in Michigan were significantly more likely to survive a hospital stay during and after the Keystone project.

These findings cannot definitively attribute the mortality reduction to the Keystone project, Pronovost says, but no other known large-scale initiatives were uniquely introduced across Michigan during the study period. "This is perhaps the only large-scale study to suggest a significant reduction in mortality from a quality-improvement initiative," Pronovost says.

The Keystone ICU Project, developed at Johns Hopkins, includes a much-heralded checklist for doctors and nurses to follow when placing a central-line catheter, highlighting five cautionary and basic steps from hand-washing to avoiding placement in the groin area where infection rates are higher. Along with the checklist, the program promotes a "culture of safety" that comprises safety science education, training in ways to identify potential safety problems, development of evidence-based solutions, and measurement of improvements. The program also empowers all caregivers, no matter how senior or junior, to question each other and stop procedures if safety is compromised.

Central lines are thin plastic tubes used regularly for patients in ICUs to administer medication or fluids, obtain blood for tests, and directly gauge cardiovascular measurements such as central venous blood pressure. But the tubes are easily contaminated.

In 2009, U.S. Health and Human Services Secretary Kathleen Sebelius called for a 50 percent reduction in catheter-related infections nationwide by 2012. To that end, in partnership with a branch of the American Hospital Association and the Michigan Hospital Association, the Johns Hopkins model is being rolled out state-by-state across the country. Forty states have launched the program, and preliminary data from some of the early adopters is very encouraging, Pronovost says. *Provided by Johns Hopkins Medical Institutions*

<http://www.electronicweeky.com/Articles/2011/01/12/50265/Windows-generate-electricity.htm>

### **Windows generate electricity**

**Steve Bush**

#### ***Using a solid electrolyte to replace liquid allows a dye-sensitised solar cell to be screen printed***

Oxford Photovoltaics has been spun out of the University of Oxford to develop solar cell windows.

From the Clarendon lab, its fundamental technology is a screen-printable solid-state dye-sensitised solar cell (DSSC). DSSCs, also known as Grätzel cells after their inventor, owe more to photosynthesis than to conventional silicon solar cells. In them, a dye and titanium dioxide are combined with an electrolyte. The dye absorbs photons, causing electrons to be transferred to the titanium dioxide, from where they can leave the cell.

"Regular DSSCs use a liquid electrolyte. We screen print the cell and the constituents set as a solid," CEO Kevin Arthur told Electronics Weekly. As such, the Oxford DSSC can be printed onto glass with no fear of it drying out. It is then capped with another sheet of glass. "One of the great advantages is that we can process it over large areas very easily," said the technology developer Dr Henry Snaith. "You don't have to worry about extensive sealing and encapsulation, which is an issue for the electrolyte dye cell."

The cells are semi-transparent, and the company is concentrating on glass substrates because it is aiming to make electricity-generating windows for buildings. So far, green-tinted is the most efficient colour, delivering 5% efficiency, although red and purple also work. "We have a roadmap with 8% cell level efficiency in 18 months, and 10% in less than three years," said CEO Arthur. No one is going to want to replace the windows of a building because its solar cells have expired. "We are looking at least 20 year life expectancy and we think we can do it," said Arthur. And they must not be too expensive. "There are no rare earths: no indium in ITO electrodes and no ruthenium," said Arthur. "We are looking to provide a system that is massively scalable."

Isis Innovation, the University's intellectual property exploitation arm, developed the initial business plan, and built the team that is now taking the company forward. "Oxford PV predicts that manufacturing costs of its product will be around 50% less than the current lowest-cost thin film technology and expects its new mechanism will eventually match the unsubsidised cost of electricity generated from fossil fuels," claimed Isis. Oxford Photovoltaics is raising funding, with Arthur expecting to close a round in March from a combination of angel and venture capital investors. The final form the company cannot be predicted with any certainty at this early stage, said Arthur: "Our preference is for an out-sourcing model with our name on the product."

<http://www.physorg.com/news/2011-02-swine-flu-vaccine-child-narcolepsy.html>

### **Swine flu vaccine likely causes child narcolepsy: study**

#### ***Children injected with the Pandemrix swine flu vaccine were nine times more likely to contract narcolepsy than those who were not vaccinated, a preliminary study by Finland's National Institute for Health and Welfare, THL, showed Tuesday.***

"Currently, the most likely explanation is that the increase in narcolepsy is by joint effect of the vaccine and some other factor(s)," THL said. The institute stressed in its preliminary study that more investigation was

needed, but said young people aged four to 19 had a "manifold increased risk of falling ill with narcolepsy" if they had been inoculated against swine flu with Pandemrix.

Finland launched an aggressive inoculation programme against the H1N1 virus in 2009, but last August THL recommended discontinuing the use of Pandemrix until it could study whether it was connected to a sharp rise in the instance of narcolepsy cases in the country, especially among children.

The European Medicines Agency also launched a probe into the suspected connection. Narcolepsy is a sleep disorder which causes extreme fatigue and often results in the patient falling soundly asleep without warning, even in the middle of an activity. Doctors in Finland reported a more than tripling of narcolepsy cases during the swine flu pandemic, and THL said "the risk of falling ill with narcolepsy among those vaccinated in the 4-19 years age group was nine-fold in comparison to those unvaccinated in the same age group."

Hospital data shows that new child narcolepsy cases in Finland jumped from seven in 2007 to 16 in 2008 to 60 during the swine flu pandemic in 2009-2010. Fifty-two of the latest cases, or 90 percent, occurred in youths who had received the Pandemrix vaccine, THL said, adding most of the patients developed narcolepsy symptoms between two and 10 weeks after being vaccinated. No changes in the number of cases were observed in children under four or youth over 19 years of age.

"The observed association (with the vaccine) is so evident that it is unlikely that other so-called confounding factors could fully explain the phenomenon," THL said, adding its next step was to evaluate if other factors had created "joint effects" with Pandemrix. So far, an unusual spike in narcolepsy patients has only been observed in Finland and Sweden despite the fact that the vaccine Pandemrix has been used on more than 90 million people in 19 countries. In Iceland, narcolepsy cases among youth also increased markedly, but this was not restricted to those who were inoculated against swine flu, said THL.

The final report from Finland's national narcolepsy task force will be released by 31st August 2011.

<http://www.bbc.co.uk/newsbeat/12325763>

### **Home DNA kits to test paternity go on sale in shops**

**By Anthony Baxter Newsbeat reporter**

#### ***Home DNA testing kits are going on sale in Boots stores across the UK later.***

Until now, the paternity packs have only been available online and in a few independent pharmacies.

The chemist says it is the first High Street shop to sell the kits, which let people settle disputes over whether someone is father to a baby without outside help. The kit costs £29.99, with an extra £129 to get the results back from the laboratory. The couple and the child each rub a cotton swab inside their mouth, put each one in a specially coloured envelope and send them off to be tested. Results are returned within five days.

DNA kits have been available online for years and in a few smaller chemists since 2009, but Boots says it's now introducing them into 375 of its stores.

#### **'Think carefully'**

Doctor Mandy Hartley from Assure DNA, the company behind the kits, says the results are "99% accurate" but warns that people should think about how they'd feel if the results don't go their way. "We really do need people to think about the impact of the test," she admits. "We encourage people to telephone us, or we telephone them and we can also put them in touch with counselling services." People thinking about a test should also know that taking someone's DNA without permission is illegal in the UK and the results aren't accepted by a court.

Child benefits campaigner, Darren Jamieson from CSAhell.com, also told Newsbeat that making the tests easily available could lead to more couples splitting up and in the long run put more pressure on the Child Support Agency. The Child Support Agency say they will only accept the results of a DNA test which has come from an approved testing provider and an approved doctor. They send all DNA testing to one chosen specialist company and they say "if a father wishes to arrange their own test there are special rules that apply."

[http://www.eurekalert.org/pub\\_releases/2011-02/ra-ae5020111.php](http://www.eurekalert.org/pub_releases/2011-02/ra-ae5020111.php)

### **An extra 5 years of life an unexpected benefit of osteoporosis treatment**

***Australian clinical researchers have noted an extraordinary and unexpected benefit of osteoporosis treatment – that people taking bisphosphonates are not only surviving well, better than people without osteoporosis, they appear to be gaining an extra five years of life.***

Associate Professor Jacqueline Center and Professor John Eisman, from Sydney's Garvan Institute of Medical Research, based their findings on data from the long running Dubbo Osteoporosis Epidemiology Study\*.

Out of a total cohort of around 2,000, a sub-group of 121 people were treated with bisphosphonates for an average of 3 years. When compared with other sub-groups taking other forms of treatment, such as Vitamin D (with or without calcium) or hormone therapy, the longer life associated with bisphosphonate treatment was marked and clear.

These findings are published in the Journal of Clinical Endocrinology and Metabolism, now online.

"While the results seemed surprisingly good, they are borne out by the data – within the limitations of any study – and appear to apply to men as well as women," said Associate Professor Center.

"When we first looked at the figures, we thought that there had to be a fallacy, that we were missing something. One of the most obvious things might be that these are people who seek medical attention, so may be healthier and live longer. So we compared the bisphosphonate group with people taking Vitamin D and calcium or women on hormone therapy."

"The comparison against these other groups of similarly health-aware people simply confirmed that our results were not skewed by that factor. In a group of women with osteoporotic fractures over the age of 75, you would expect 50% to die over a period of five years. Among women in that age group who took bisphosphonates, the death rate dropped to 10%. Similarly, in a group of younger women, where you would expect 20-25% to die over 5 years, there were no deaths."

"The data were consistent with about a 5 year survival advantage for people on bisphosphonates." The authors are intrigued by their findings. "We speculate that it may have something to do with the fact that bone acts as a repository for toxic heavy metals such as lead and cadmium," said Professor Eisman. "So when people get older, they lose bone. When this happens, these toxic materials are released back into the body and may adversely affect health."

"By preventing bone loss, bisphosphonates prevent some of this toxic metal release. While we know that this is the case, we don't yet have evidence that this produces the survival benefit."

Osteoporosis is a serious and disabling condition that affects around 2 million Australians. Someone is admitted to hospital with an osteoporotic fracture every 5-6 minutes, averaging 262 hospitalisations each day. It has already been shown by Garvan and others that osteoporotic fractures increase a person's risk of dying, even after relatively minor fractures if that person is elderly.

"Osteoporosis is a big societal burden and remains a poorly understood and severely undertreated disease in Australia," said Eisman. "Only about 30% of women and 10% of men with osteoporosis receive treatment, which is unacceptable when you consider that people could be helped, and death could be delayed by several years. There is good evidence – even without this study - that treating osteoporosis reduces fractures and reduces mortality."

"While osteoporosis is clearly under-recognised and under-treated, the findings of this study are important to better understanding the benefits of these treatments and may directly influence doctors' practice. It was unexpected and remarkable to find that not only osteoporosis but also life expectancy appear to be improved for people taking bisphosphonates," said Dr Christine Bennett, Chair of the Bupa Health Foundation Steering Committee and Bupa Australia's Chief Medical Officer.

"Bupa Health Foundation is proud to have supported this valuable research since 2005 and we see its findings as a major breakthrough that can now guide doctors' treatment decisions for these very vulnerable older people." Like any pharmaceutical product, bisphosphonates may have unpredictable side effects in a small minority of people and should only be used for their approved purpose.

*\*Dubbo Osteoporosis Epidemiology Study*

*The Dubbo Osteoporosis Epidemiology Study is an ongoing population-based study that started in 1989 in Dubbo, a city with a population of 32,000 in regional New South Wales. The study cohort is women (1223) and men (898) over the age of 60.*

*Approximately 60% of eligible people were recruited into the study.*

**ACKNOWLEDGEMENTS AND DISCLOSURE SUMMARY**

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*Associate Professor Center has been supported by and/or has given educational talks for Eli Lilly, Merck Sharp and Dohme, Novartis and Sanofi-Aventis. Professor Eisman has consulted for and/or received research funding from Amgen, deCode, Eli Lilly, Merck Sharp and Dohme, Novartis, Sanofi-Aventis and Servier. The other authors on the paper have nothing to disclose.*

[http://www.eurekalert.org/pub\\_releases/2011-02/jgh-fnc020111.php](http://www.eurekalert.org/pub_releases/2011-02/jgh-fnc020111.php)

### **First new C. difficile drug in a generation superior to existing treatments: Researchers Significantly reduces recurrence of infection, improves cure rates**

Clostridium difficile infection (CDI) is a significant and growing problem in hospitals and other health care facilities, but no new drugs to treat the condition have been developed in several decades. However, a large-scale, phase 3 trial conducted by Canadian and U.S. researchers shows that the new antibiotic Fidaxomicin is superior to existing treatments, demonstrating a 45 percent reduction in recurrences vs. the existing licensed treatment. Their results were published in February, 2011 in The New England Journal of Medicine.

"There wasn't much interest in *C. difficile* for many years, because it wasn't considered a serious disease," said study co-author Dr. Mark A. Miller, head of the Division of Infectious Diseases and Chief of Microbiology at the Jewish General Hospital in Montreal, and a clinical investigator at the Lady Davis Institute for Medical Research. "However, over the past decade the bacterium has mutated into something much more serious that has caused epidemics worldwide. It is particularly notorious for recurrences. About 20 to 30 percent of patients suffer relapses. Recurrent *C. difficile* is very difficult to treat, and this has spurred interest in newer and better treatments."

Fidaxomicin, developed by Optimer Pharmaceuticals of San Diego, is the first in a new class of narrow-spectrum macrocyclic antibiotics. It is only minimally absorbed from the gut into the bloodstream and is specifically targeted at *C. difficile* in the intestine. Thus the drug acts by killing *C. difficile* bacteria without affecting the beneficial flora in the human gut which help stave off recurrences.

A total of 629 patients were enrolled in the multicentre, double-blind, randomized, parallel-group trial conducted between May 9, 2006, and August 21, 2008. They received Fidaxomicin (200 mg twice daily) or the antibiotic vancomycin (125 mg four times daily) orally for 10 days. Vancomycin was first developed in the 1950s, and to date is the only FDA- and Health Canada-approved treatment for CDI.

"These results showed that recurrence of CDI is significantly less likely to occur following treatment with Fidaxomicin versus vancomycin," said lead author, Thomas J. Louie, M.D., Medical Director, Infection Prevention and Control for the Calgary Health Region and professor in the Departments of Medicine and Microbiology-Infectious Diseases, University of Calgary.

"Anybody who knows *C. difficile* recognizes that recurrences are the major problem with this disease," agreed Dr. Miller, also assistant professor in Medicine, Microbiology and Immunology at McGill University. "Anything that can reduce the recurrence rate, especially as dramatically as Fidaxomicin, is a very important milestone in the treatment of *C. difficile*."

[http://www.eurekalert.org/pub\\_releases/2011-02/plos-fof013111.php](http://www.eurekalert.org/pub_releases/2011-02/plos-fof013111.php)

### **Flash of fresh insight by electrical brain stimulation**

***Are we on the verge of being able to stimulate the brain to see the world anew - an electric thinking cap?***

Research by Richard Chi and Allan Snyder from the Centre for the Mind at the University of Sydney suggests that this could be the case. They found that participants who received electrical stimulation of the anterior temporal lobes were three times as likely to reach the fresh insight necessary to solve a difficult, unfamiliar problem than those in the control group. The study published on February 2 in the open-access journal PLoS ONE.

According to the authors, our propensity to rigidly apply strategies and insights that have had previous success is a major bottleneck to making creative leaps in solving new problems. There is normally a cognitive tradeoff between the necessity of being fast at the familiar on one hand and being receptive to novelty on the other.

Chi and Snyder argue that we can modulate this tradeoff to our advantage by applying transcranial direct current stimulation (tDCS), a safe, non-invasive technique that temporarily increases or decreases excitability of populations of neurons. In particular, tDCS can be used to manipulate the competition between the left and right hemisphere by inhibiting and/or disinhibiting certain networks. Their findings are consistent with evidence that the right anterior temporal lobe is associated with insight or novel meaning and that inhibition of the left anterior temporal lobe can induce a cognitive style that is less top-down, less influenced by preconceptions.

While further studies involving brain stimulation in combination with neuroimaging are needed to elucidate the exact mechanisms leading to insight, Chi and Snyder can imagine a future when non-invasive brain stimulation is briefly employed for solving problems that have evaded traditional cognitive approaches.

Citation: Chi RP, Snyder AW (2011) Facilitate Insight by Non-Invasive Brain Stimulation. PLoS ONE 6(2): e16655. doi:10.1371/journal.pone.0016655

[http://www.eurekalert.org/pub\\_releases/2011-02/haog-mmm020211.php](http://www.eurekalert.org/pub_releases/2011-02/haog-mmm020211.php)

### **Malaria medication may help against 1 type of frontotemporal dementia**

***Frontotemporal dementia is caused by a breakdown of nerve cells in the frontal and temporal region of the brain (fronto-temporal lobe), which leads to, among other symptoms, a change in personality and behavior.***

The cause of some forms of frontotemporal dementia is a genetically determined reduction of a hormone-like growth factor, progranulin. Scientists around Dr. Anja Capell and Prof. Christian Haass have now shown that various drugs that are already on the market to treat malaria, angina pectoris or heart rhythm disturbances can increase the production of progranulin. Accordingly, these drugs are good candidates for treatment of this



specific form of frontotemporal dementia. The work will be published in the online edition of the scientific journal *Journal of Neuroscience* on February 2nd, 2011.

Progranulin is needed in the human brain as a protective factor for sensitive nerve cells, too little progranulin therefore results in a progressive neuronal cell death. As for almost every other gene, there are also two copies of the progranulin gene in the cell. In patients with progranulin dependent frontotemporal dementia, one of the two copies is defective, leading to a 50% reduction in progranulin levels. To rescue the lack of progranulin, the Munich researchers tested various substances for their ability to stimulate the remaining progranulin production and identified a drug called bafilomycin (BafA1). They then examined the molecular mechanism underlying the impact of BafA1 on progranulin more closely. Growth factors such as progranulin are produced in cellular membrane inclusions, known as vesicles. BafA1 has an alkalizing effect on these vesicles: After administration of BafA1 the interior of the vesicles is less acidic – and this increases the production of progranulin.

This observation encouraged the researchers to investigate further alkalizing substances for their ability to raise progranulin levels. Among the substances that passed the test were three drugs that are already on the market to treat various diseases: a medication for angina pectoris (bepridil), one for heart rhythm problems (amiodarone) and the widely used malaria drug chloroquine. Chloroquine increased the progranulin level not only in experiments with mouse cells to normal, but also in cells from patients with the defective progranulin gene.

In a clinical study in collaboration with the University of London, the team of Prof. Haass and Dr. Capell will now investigate whether chloroquine actually helps against progranulin dependent frontotemporal dementia. The human studies can be started very soon, as chloroquine has been used on countless patients, so that serious side effects are not to be expected. Even though the Munich scientists are optimistic, Prof. Haass warns against exaggerated hopes. "Experience shows that the step from cell and animal models to the patient is always connected with considerable difficulties. It will take several years until we know, whether chloroquine can be used as therapy for progranulin dependent frontotemporal dementia," says Haass.

*Original publication: Capell, A., Liebscher, S., Fellerer, K., Brouwers, N., Willem, M., Lammich, S., Gijssels, I., Bittner, T., Carlson, A.M., Sasse, F., Kunze, B., Steinmetz, H., Jansen, R., Dormann, D., Sleegers, K., Cruts, M., Herms, J., Van Broeckhoven, C., Haass, C. (2011). Rescue of Progranulin Deficiency Associated with Frontotemporal Lobar Degeneration by Alkalizing Reagents and Inhibition of Vacuolar ATPase. *J. Neurosci.*, published online on February 2nd, 2011.*

DOI:10.1523/JNEUROSCI.5757-10.2011

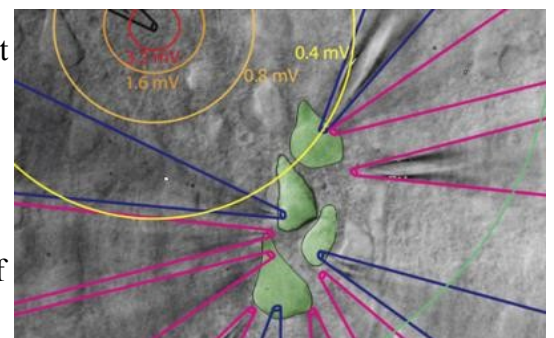
[http://www.eurekalert.org/pub\\_releases/2011-02/ciot-nft020211.php](http://www.eurekalert.org/pub_releases/2011-02/ciot-nft020211.php)

## **Neurobiologists find that weak electrical fields in the brain help neurons fire together** **Coordinated behavior occurs whether or not neurons are actually connected via synapses**

Pasadena, Calif. - The brain - awake and sleeping - is awash in electrical activity, and not just from the individual pings of single neurons communicating with each other. In fact, the brain is enveloped in countless overlapping electric fields, generated by the neural circuits of scores of communicating neurons. The fields were once thought to be an "epiphenomenon, a 'bug' of sorts, occurring during neural communication," says neuroscientist Costas Anastassiou, a postdoctoral scholar in biology at the California Institute of Technology (Caltech). New work by Anastassiou and his colleagues, however, suggests that the fields do much more - and that they may, in fact, represent an additional form of neural communication.

"In other words," says Anastassiou, the lead author of a paper about the work appearing in the journal *Nature Neuroscience*, "while active neurons give rise to extracellular fields, the same fields feed back to the neurons and alter their behavior," even though the neurons are not physically connected - a phenomenon known as ephaptic coupling.

"So far, neural communication has been thought to occur at localized machines, termed synapses. Our work suggests an additional means of neural communication through the extracellular space independent of synapses."



***Ephaptic coupling leads to coordinated spiking of nearby neurons, as measured using a 12-pipette electrophysiology setup developed in the laboratory of coauthor Henry Markram. Image from Figure 4 in Anastassiou et., Nature Neuroscience, 2011***

Extracellular electric fields exist throughout the living brain, though they are particularly strong and robustly repetitive in specific brain regions such as the hippocampus, which is involved in memory formation, and the neocortex, the area where long-term memories are held. "The perpetual fluctuations of these extracellular fields are the hallmark of the living and behaving brain in all organisms, and their absence is a strong indicator of a deeply comatose, or even dead, brain," Anastassiou explains.

Previously, neurobiologists assumed that the fields were capable of affecting - and even controlling - neural activity only during severe pathological conditions such as epileptic seizures, which induce very strong fields. Few studies, however, had actually assessed the impact of far weaker - but very common - non-epileptic fields. "The reason is simple," Anastassiou says. "It is very hard to conduct an in vivo experiment in the absence of extracellular fields," to observe what changes when the fields are not around.

To tease out those effects, Anastassiou and his colleagues, including Caltech neuroscientist Christof Koch, the Lois and Victor Troendle Professor of Cognitive and Behavioral Biology and professor of computation and neural systems, focused on strong but slowly oscillating fields, called local field potentials (LFP), that arise from neural circuits composed of just a few rat brain cells. Measuring those fields and their effects required positioning a cluster of tiny electrodes within a volume equivalent to that of a single cell body - and at distances of less than 50 millionths of a meter from one another.

"Because it had been so hard to position that many electrodes within such a small volume of brain tissue, the findings of our research are truly novel," Anastassiou says. Previously, he explains, "nobody had been able to attain this level of spatial and temporal resolution."

An "unexpected and surprising finding was how already very weak extracellular fields can alter neural activity," he says. "For example, we observed that fields as weak as one millivolt per millimeter robustly alter the firing of individual neurons, and increase the so-called "spike-field coherence" - the synchronicity with which neurons fire with relationship to the field." "In the mammalian brain, we know that extracellular fields may easily exceed two to three millivolts per millimeter. Our findings suggest that under such conditions, this effect becomes significant."

What does that mean for brain computation? "Neuroscientists have long speculated about this," Anastassiou says. "Increased spike-field coherency may substantially enhance the amount of information transmitted between neurons as well as increase its reliability. Moreover, it has been long known that brain activity patterns related to memory and navigation give rise to a robust LFP and enhanced spike-field coherency. We believe ephaptic coupling does not have one major effect, but instead contributes on many levels during intense brain processing."

Can external electric fields have similar effects on the brain? "This is an interesting question," Anastassiou says. "Indeed, physics dictates that any external field will impact the neural membrane. Importantly, though, the effect of externally imposed fields will also depend on the brain state. One could think of the brain as a distributed computer - not all brain areas show the same level of activation at all times.

"Whether an externally imposed field will impact the brain also depends on which brain area is targeted. During epileptic seizures, pathological fields can be as strong as 100 millivolts per millimeter - such fields strongly entrain neural firing and give rise to super-synchronized states." And that, he adds, suggests that electric field activity - even from external fields - in certain brain areas, during specific brain states, may have strong cognitive and behavioral effects.

Ultimately, Anastassiou, Koch, and their colleagues would like to test whether ephaptic coupling affects human cognitive processing, and under which circumstances. "I firmly believe that understanding the origin and functionality of endogenous brain fields will lead to several revelations regarding information processing at the circuit level, which, in my opinion, is the level at which percepts and concepts arise," Anastassiou says. "This, in turn, will lead us to address how biophysics gives rise to cognition in a mechanistic manner - and that, I think, is the holy grail of neuroscience."

*The work in the paper, "Ephaptic coupling of cortical neurons," published January 16 in the advance online edition of the journal, was supported by the Engineering Physical Sciences Research Council, the Sloan-Swartz Foundation, the Swiss National Science Foundation, EU Synapse, the National Science Foundation, the Mathers Foundation, and the National Research Foundation of Korea.*

*Written by Kathy Svitil*

[http://www.eurekalert.org/pub\\_releases/2011-02/wuso-nnm020211.php](http://www.eurekalert.org/pub_releases/2011-02/wuso-nnm020211.php)

### **New nanoparticles make blood clots visible**

***For almost two decades, cardiologists have searched for ways to see dangerous blood clots before they cause heart attacks.***

Now, researchers at Washington University School of Medicine in St. Louis report that they have designed nanoparticles that find clots and make them visible to a new kind of X-ray technology.

According to Gregory Lanza, MD, PhD, a Washington University cardiologist at Barnes-Jewish Hospital, these nanoparticles will take the guesswork out of deciding whether a person coming to the hospital with chest pain is actually having a heart attack.

"Every year, millions of people come to the emergency room with chest pain. For some of them, we know it's not their heart. But for most, we're not sure," says Lanza, a professor of medicine. When there is any doubt, the patient must be admitted to the hospital and undergo tests to rule out or confirm a heart attack.

"Those tests cost money and they take time," Lanza says. Rather than an overnight stay to make sure the patient is stable, this new technology could reveal the location of a blood clot in a matter of hours.

### Spectral CT

The nanoparticles are designed to be used with a new type of CT scanner that is capable of "seeing" metals in color. The new technology, called spectral CT, uses the full spectrum of the X-ray beam to differentiate objects that would be indistinguishable with a regular CT scanner that sees only black and white.

Lanza says the new scanner takes advantage of the same physics that astronomers use to look at the light from a star and tell what metals it contains. "They're looking at the X-ray spectrum, and the X-ray spectrum tells them what metals are there," he says. "That's exactly what we do."

### Bismuth nanoparticles

In this case, the metal in question is bismuth. Dipanjan Pan, PhD, research assistant professor of medicine, designed a nanoparticle that contains enough bismuth for it to be seen by the spectral CT scanner.

"Each nanoparticle is carrying a million atoms of bismuth," Lanza says. Since CT is a relatively insensitive imaging technique, this sheer quantity of metal is necessary for the particles to be visible to the scanner.

But bismuth is a toxic heavy metal, Pan says. It can't be injected into the body on its own. Instead, Pan used a compound made of bismuth atoms attached to fatty acid chains that can't come apart in the body. He then dissolved this compound in a detergent and encapsulated the mixture in a phospholipid membrane. Much like oil droplets suspended in a shaken vinaigrette, these particles self-assemble with the bismuth compound at the core.

As Pan showed in a mouse model, the design of the nanoparticles also allows the body to break them apart and release the inner bismuth compound in a safe form.

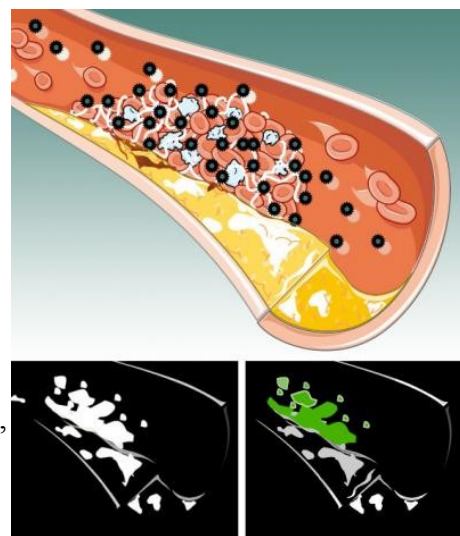
Once the nanoparticles carried enough bismuth to be visible to the scanner, Pan added a molecule to the particles' surface that seeks out a protein called fibrin. Fibrin is common in blood clots but is not found elsewhere in the vasculature.

"If you're having a heart attack, the lining of your coronary artery has ruptured, and a clot is forming to repair it," Lanza says. "But that clot is starting to narrow the vessel so blood can't get by. Now we have a nanoparticle that will see that clot."

A spectral CT image with the bismuth nanoparticles targeted to fibrin will provide the same information as a traditional black and white CT image, but the fibrin in any blood clots will show up in a color, such as yellow or green, solving the problem of calcium interference common to traditional CT scanners.

The spectral CT scanner used in this study is still a prototype instrument, developed by Philips Research in Hamburg, Germany. The nanoparticles have only been tested in rabbits and other animal models, but early results show success in distinguishing blood clots from calcium interference.

*A blood vessel (top) with ruptured atherosclerotic plaque, shown in yellow, is developing a blood clot. The nanoparticles, shown in blue and black, are targeted to a protein in the blood clot called fibrin, shown in light blue. A traditional CT image, bottom left, shows no difference between the blood clot and the calcium in the plaque, making it unclear whether this image shows a clot that should be treated. A spectral CT image, bottom right, "sees" the bismuth nanoparticles targeted to fibrin in green, differentiating it from calcium, still shown in white, in the plaque. Wiley-VCH Verlag GmbH & Co. KGaA.*



### Saving lives

More than simply confirming a heart attack, the new nanoparticles and spectral CT scanner can show a clot's exact location.

Today, even if doctors determine the patient is having a heart attack, they can't locate the clot without admitting the patient to the cardiac catheterization lab, inserting a dye and looking for narrow plaque-filled arteries they could open with stents. But Lanza says looking for narrow arteries doesn't solve all the problems.

"The ones that have very narrow openings are not the worrisome ones," Lanza says. "We find those in the cardiac catheterization lab and we open them up."

What is worrisome is when blood is free to flow through the arteries, but there is unstable plaque on the artery wall, what Lanza calls "moderate-grade disease."

"Most people's heart attacks or strokes are from moderate-grade disease that breaks off and all of a sudden blocks an artery," Lanza says. "It's what happened to NBC newsman Tim Russert. You need something that tells you there is ruptured plaque even when the vessel isn't very narrow."

Since this nanoparticle finds and sticks to fibrin in the vessels, it would allow doctors to see problems that were previously difficult or impossible to detect.

With this imaging technique, Lanza predicts new approaches to treating coronary disease. Unstable plaque that doesn't restrict much blood flow does not require an expensive stent to prop the vessel open. Instead, Lanza foresees technologies that might act like Band-Aids, sealing weak spots in the vessel walls.

"Today, you wouldn't know where to stick the Band-Aid," Lanza says. "But spectral CT imaging with bismuth nanoparticles would show the exact location of clots in the vessels, making it possible to prevent the dangerous rupture of unstable plaque."

*Pan D, Roessl E, Schlomka JP, Caruthers SD, Senpan A, Scott MJ, Allen JS, Zhang H, Hu G, Gaffney PJ, Choi ET, Rasche V, Wickline SA, Proksa R, Lanza GM. Computed Tomography in color: NanoK-enhanced spectral CT molecular imaging. Angewandte Chemie, International Edition, Dec. 10, 2010.*

*This work was supported by grants from the American Heart Association, National Cancer Institute, Bioengineering Research Partnership and the National Heart, Lung, and Blood Institute.*

*The spectral CT prototype is on loan to Washington University from Philips Research in Hamburg, Germany, for codevelopment of the scanner, software and nanoparticles.*

[http://www.eurekalert.org/pub\\_releases/2011-02/uol-pbp020211.php](http://www.eurekalert.org/pub_releases/2011-02/uol-pbp020211.php)

### **Prehabilitation better prepares patients for knee replacement surgery**

***An exercise program designed by researchers at the University of Louisville for patients with severe knee arthritis improves leg strength and patients' functional ability before knee replacement surgery, according to recent report in The Journal of Strength and Conditioning Research.***

The study, led by UofL's Ann Swank, Ph.D., CSCS, and Robert Topp, Ph.D., R.N., says gains from exercise before knee replacement or prehabilitation may translate into improved recovery after surgery.

"We designed this program to be easily transferred to a home environment," Swank said. "It is very possible for many patients preparing for knee replacement surgery to participate in this exercise program and experience increased strength and functionality such as getting up from a chair or climbing stairs."

However, Swank noted the prehabilitation program did not significantly improve functional tasks such as walking speed or going downstairs.

The study included 71 patients scheduled for knee replacement surgery because of severe osteoarthritis that could not be managed with pain medications. Osteoarthritis of the knee is a very common condition in older adults, causing pain and gradual declines in the ability to perform everyday tasks. When pain becomes so severe that medications no longer provide relief, knee replacement surgery is the only option. By that time, reduced leg strength may be present for several years - not only decreasing functional ability, but increasing the risk of falls.

One group of participants was randomly assigned to a comprehensive prehabilitation program, consisting of light resistance training, flexibility and step exercise, and light walking.

Patients in this "pre-rehab" group exercised three times per week, in the clinic and at home, for four to eight weeks before knee replacement surgery. Patients in the comparison group received standard preoperative care, with instructions to continue their usual activities. The two groups were compared for knee strength and performance on standard functional tests.

When tested one week before surgery, patients who went through the prehabilitation program showed improvements in several areas. In particular, they had a 10 percent increase in extension strength in the leg scheduled for knee replacement. In contrast, the comparison group had a 10 percent decrease in extension strength. In addition, patients in the prehabilitation group had less pain when performing the functional tests. For patients receiving standard care, performance on some functional tests actually decreased in the weeks before surgery - possibly reflecting increased pain scores.

The results show significant improvements in strength and functioning in the weeks before knee replacement surgery. Strengthening of the leg undergoing knee replacement may be a particularly important factor - exercise may reduce the strength imbalance between legs, therefore contributing to the functional improvement. The researchers do note that even with exercise, the surgical leg remains significantly weaker than the other leg.

Previous studies have evaluated exercise programs to improve leg strength and functional ability before knee replacement surgery, but with limited success. Although the study did not compare postoperative recovery, increases in leg strength and performance of functional tasks before knee replacement surgery may result in

improved postoperative recovery because preoperative performance of functional tasks has been shown to be a predictor of postoperative performance of functional tasks, Swank said.

Topp noted that in addition to the clinical aspects, there is the potential for cost-savings as well.

"The next step in this research is to determine whether this comprehensive prehabilitation exercise program translates to a savings in healthcare dollars," Topp said. "For example, reducing the number of days a patient stays in the hospital or reducing the number of physical therapy sessions."

*Several other University of Louisville faculty also contributed to the study, "Prehabilitation Before Total Knee Arthroplasty Increases Strength and Function in Older Adults With Severe Osteoarthritis."*

[http://www.eurekalert.org/pub\\_releases/2011-02/ps-rme020211.php](http://www.eurekalert.org/pub_releases/2011-02/ps-rme020211.php)

### **Ritalin may ease early iron deficiency damage**

***Ritalin may help improve brain function in adolescent rats that were iron deficient during infancy, according to a team of Penn State neuroscientists. This may have implications for iron-deficient human infants as well.***

The researchers found that low doses of Ritalin can help improve the focus of iron-deficient rats. Higher doses proved to hurt rather than help the control animals' focus, making them hyperactive. The control rats that were not iron deficient but received low doses of Ritalin showed no positive or negative change in performance.

When children are deprived of iron at any point during the last trimester of pregnancy or the first six months of life - a critical period of brain development - they suffer brain damage at least through early adulthood, and possibly beyond. In particular, their motor function can be impaired as well as their ability to focus.

Children with iron deficiency can exhibit attention problems, attachment issues and motor problems, said Byron C. Jones, professor of biobehavioral health. Iron-deficient adults often have restless leg syndrome. People who become iron deficient after three years of age can recover by taking iron supplements.

According to the Centers for Disease Control and Prevention, iron deficiency ranks in the top 10 causes of global disease and affects more than 2 billion children.

Iron-deficient adolescent rats were treated with methylphenidate, commonly known as Ritalin, to see if the drug would help the animals overcome the deficit, as reported in this quarter's issue of Behavioural Brain Research.

"Most of the research community knows that iron deficiency has a major hit on dopamine systems," said Jones. "Why hasn't anybody tried a dopamine drug to repair or at least rescue some of what's lost?" Ritalin is a drug that helps regulate levels of dopamine in the brain. Most often it is prescribed to patients with attention-deficit/hyperactivity disorder. Dopamine is important in controlling many important functions of the brain, like being able to sustain attention and shift it.

The researchers made half the rats in the test group iron deficient beginning four days after birth, mimicking a human infant deprived of iron during brain development. Once weaned, the rats were put on iron-sufficient diets. At 45 days, when the rats reached adolescence, the researchers tested the rats' ability to remember, respond, sustain attention and then shift attention. For every test, they gave the rats two different bowls to dig in. In each case only one bowl contained food, but the bowls were filled with either coarse or fine gravel. Before receiving any Ritalin, each rat had time to explore the bowls and find the food.

The researchers then broke the rats into four groups, with control and iron-deficient rats in all four groups. One group served as the control, receiving no Ritalin. They gave the other three groups different amounts of Ritalin. After 15 days on the medication, the researchers retested the rats, seeing if the rats could find the food in either filler. The test was complicated by the addition of either mint or strawberry scents.

"Ritalin may not be the best drug - but it's shown that we can in fact treat some of the effects" of early-life iron deficiency, Jones said.

According to Jones, these were the first experiments with Ritalin and iron deficiency. The team plans to conduct further research. "We're looking now to see if in fact their brains are going to show any recovery, but there's no evidence so far in terms of (recovery of) the dopamine receptors," Jones said.

*Also working on this research were Wael M.Y. Mohamed, graduate student in neuroscience; Erica L. Unger, research associate in nutritional science; and Sarita K. Kambhampati, undergraduate student in pre-medicine.*

[http://www.eurekalert.org/pub\\_releases/2011-02/uoc-ssp012811.php](http://www.eurekalert.org/pub_releases/2011-02/uoc-ssp012811.php)

### **Six small planets orbiting a sun-like star amaze astronomers**

***SANTA CRUZ, CA-A remarkable planetary system discovered by NASA's Kepler mission has six planets around a Sun-like star, including five small planets in tightly packed orbits.***

Astronomers at the University of California, Santa Cruz, and their coauthors analyzed the orbital dynamics of the system, determined the sizes and masses of the planets, and figured out their likely compositions-all based on Kepler's measurements of the changing brightness of the host star (called Kepler-11) as the planets passed in front of it.

"Not only is this an amazing planetary system, it also validates a powerful new method to measure the masses of planets," said Daniel Fabrycky, a Hubble postdoctoral fellow at UC Santa Cruz, who led the orbital dynamics analysis. Fabrycky and Jack Lissauer, a scientist at NASA Ames Research Center in Mountain View, are the lead authors of a paper on Kepler-11 published in the February 3 issue of Nature.

The five inner planets in the Kepler-11 system range in size from 2.3 to 13.5 times the mass of the Earth. Their orbital periods are all less than 50 days, so they orbit within a region that would fit inside the orbit of Mercury in our solar system. The sixth planet is larger and farther out, with an orbital period of 118 days and an undetermined mass.

"Of the six planets, the most massive are potentially like Neptune and Uranus, but the three lowest mass planets are unlike anything we have in our solar system," said Jonathan Fortney, assistant professor of astronomy and astrophysics at UCSC, who led the work on understanding the structure and composition of the planets, along with UCSC graduate students Eric Lopez and Neil Miller.

The Kepler space telescope detects planets that "transit" or pass in front of their host star, causing periodic dips in the brightness of the star as measured by the telescope's sensitive photometer. The amount of the brightness reduction tells scientists how big the planet is in terms of its radius. The time between transits tells them its orbital period. To determine the planets' masses, Fabrycky analyzed slight variations in the orbital periods caused by gravitational interactions among the planets.

"The timing of the transits is not perfectly periodic, and that is the signature of the planets gravitationally interacting," he said. "By developing a model of the orbital dynamics, we worked out the masses of the planets and verified that the system can be stable on long time scales of millions of years."

Previously, detections of transiting planets have been followed up with observations from powerful ground-based telescopes to confirm the planet and determine its mass using Doppler spectroscopy, which measures the "wobble" in the motion of the star caused by the gravitational tug of the planet. With Kepler-11, however, the planets are too small and the star (2,000 light-years away) is too faint for Doppler spectroscopy to work. This is likely to be the case with many of the planets detected by the Kepler mission, the main goal of which is to find small, Earth-size planets in the habitable zones of their stars.

"We will need to use orbital dynamics a lot with the Kepler mission to measure the masses of planets, so we expect to be doing a lot of those analyses," Fabrycky said.

More than 100 transiting planets have been observed by Kepler and other telescopes, but the vast majority of them are Jupiter-like gas giants, and almost all of them are in single-planet systems. The Kepler-11 system is remarkable in terms of the number of planets, their small sizes, and their closely packed orbits. Before this, astronomers had determined both size and mass for only three exoplanets smaller than Neptune. Now, a single planetary system has added five more. The sixth planet in Kepler-11 is separated enough from the others that the orbital perturbation method can't be used to determine its mass, Fabrycky said.

As is the case in our solar system, all of the Kepler-11 planets orbit in more or less the same plane. This finding reinforces the idea that planets form in flattened disks of gas and dust spinning around a star, and the disk pattern is conserved after the planets have formed, Fabrycky said. "The coplanar orbits in our solar system inspired this theory in the first place, and now we have another good example. But that and the Sun-like star are the only parts of Kepler-11 that are like the solar system," he said.

The densities of the planets (derived from mass and radius) provide clues to their compositions. All six planets have densities lower than Earth's. "It looks like the inner two could be mostly water, with possibly a thin skin of hydrogen-helium gas on top, like mini-Neptunes," Fortney said. "The ones farther out have densities less than water, which seems to indicate significant hydrogen-helium atmospheres."

That's surprising, because a small, hot planet should have a hard time holding onto a lightweight atmosphere. "These planets are pretty hot because of their close orbits, and the hotter it is the more gravity you need to keep the atmosphere," Fortney said. "My students and I are still working on this, but our thoughts are that all these planets probably started with more massive hydrogen-helium atmospheres, and we see the remnants of those atmospheres on the ones farther out. The ones closer in have probably lost most of it."

One reason a six-planet system is so exciting is that it allows scientists to make these kinds of comparisons among planets within the same system. "That's really powerful, because we can work out what's happened to this system as a whole," Fortney said. "Comparative planetary science is how we've come to understand our solar system, so this is much better than just finding more solitary hot Jupiters around other stars."

For example, the presence of small planets with hydrogen-helium atmospheres suggests that this system formed relatively quickly, he said. Studies indicate that stellar disks lose their hydrogen and helium gas within about 5 million years. "So it tells us how quickly planets can form," Fortney said.

The inner planets are so close together that it seems unlikely they formed where they are now, he added. "At least some must have formed farther out and migrated inward. If a planet is embedded in a disk of gas, the drag on it leads to the planet spiralling inward over time. So formation and migration had to happen early on."

*The Nature paper's 39 coauthors include scientists at 16 institutions. This research was funded by NASA.*

[http://www.eurekalert.org/pub\\_releases/2011-02/qmuo-wfa020111.php](http://www.eurekalert.org/pub_releases/2011-02/qmuo-wfa020111.php)

### **Why folic acid may prevent a first heart attack, but not a second**

***A perplexing medical paradox now has an explanation according to research undertaken at Barts and The London School of Medicine and Dentistry and published in the current issue of the Public Library of Science.***

The paradox is that taking folic acid, a B vitamin, lowers homocysteine in the blood which, epidemiological evidence indicates, should lower the risk of heart attack, but clinical trials of folic acid have not shown the expected benefit.

The explanation is surprisingly simple; lowering homocysteine prevents platelets sticking, which stops blood clots... something aspirin also does, so if people in the trials were already taking aspirin there would be no extra benefit in lowering homocysteine with folic acid. Aspirin was in fact widely used by participants in the trials because they were mainly conducted in patients who had already had a heart attack or other cardiovascular diseases.

Research led by Dr David Wald at the Wolfson Institute of Preventive Medicine at Barts and The London School of Medicine and Dentistry showed that there was a difference in the reduction in heart disease events between the five trials with the lowest aspirin use (60 per cent of the participants took aspirin) and the five trials with the highest use (91 per cent took aspirin). The observed risk reduction was six per cent but it would have been 15 per cent if no one had been taking aspirin. Research was based on 75 epidemiological studies involving about 50,000 participants and clinical trials involving about 40,000 participants.

"The explanation has important implications," said Dr David Wald, the lead author of the paper. "The negative clinical trial evidence should not close the door on folic acid – folic acid may still be of benefit in people who have not had a heart attack because they will generally not be taking aspirin".

*'Reconciling the evidence on serum homocysteine and ischaemic heart disease: a meta-analysis' is published in the Public Library of Science (PLOS One), 2 February 2011.*

<http://www.physorg.com/news/2011-02-migraine-surgery-good-long-term-outcomes.html>

### **Migraine surgery offers good long-term outcomes**

***Surgery to "deactivate" migraine headaches produces lasting good results, with nearly 90 percent of patients having at least partial relief at five years' follow-up, reports a study in the February issue of Plastic and Reconstructive Surgery®, the official medical journal of the American Society of Plastic Surgeons (ASPS).***

In about 30 percent of patients, migraine headaches were completely eliminated after surgery, according to the new study, led by Dr. Bahman Guyuron, chairman of Plastic and Reconstructive Surgery at University Hospitals Case Medical Center and Case Western Reserve University School of Medicine in Cleveland, Ohio. **'Trigger Site' Surgery Reduces or Eliminates Migraine Headaches**

Dr. Guyuron, a plastic surgeon, developed the migraine surgery techniques after noticing that some migraine patients had reduced headache activity after undergoing cosmetic forehead-lift procedures. The techniques consist of "surgical deactivation" of "trigger sites" in the muscles or nerves that produce pain.

For example, for patients with frontal migraine headaches starting in the forehead, the muscles in that area were removed, as in forehead-lift surgery. This procedure may reduce headache attacks by relieving pressure on key nerve in the frontal area. Other approaches target other migraine trigger sites.

Before surgery, each patient was tested with botulinum toxin A (Botox) to confirm the correct trigger sites. For most patients, surgery targeted at least two trigger sites. The five-year results - including standard measures of migraine-related pain, disability, and quality of life - were evaluated in 69 patients.

Eighty-eight percent of these patients had a positive long-term response to surgery. Headaches were significantly decreased in 59 percent of patients, and completely eliminated in 29 percent. The remaining patients had no change in headache activity.

Migraine attacks were less frequent after surgery; average migraine frequency decreased from about eleven to four per month. When attacks occurred, they didn't last as long - average duration decreased from 34 to eight hours. Migraine surgery also led to significant improvements in quality of life, with few serious adverse effects.

Migraine is a very common problem that interferes with many aspects of daily life for millions of Americans. About one-third of patients are not helped by current treatments. The new surgical techniques have

the potential to reduce or eliminate migraine attacks for many patients who do not respond to other treatments. A previous study found good results at one-year follow-up evaluation.

The new report shows that these good outcomes are maintained through five years' follow-up. The findings "provide strong evidence that surgical deactivation of one or more trigger sites can successfully eliminate or reduce the frequency, duration, and intensity of migraine headache, and the results are enduring," Dr. Guyuron and colleagues write. More research will be needed to refine the surgical techniques - as well as to clarify the reasons for the effectiveness of surgical deactivation of trigger sites in relieving migraine headaches.

*Provided by University Hospitals Case Medical Center*

<http://www.newscientist.com/article/mg20927983.800-undiagnosed-diseases-program-finds-rare-new-disorder.html>

### **Undiagnosed Diseases Program finds rare new disorder**

***AN 18-month wait for a diagnosis might seem extreme, but not when the medical disorder in question was formerly unknown.***

In 2008, the US National Institutes of Health established the Undiagnosed Diseases Program (UDP) to help people with mysterious conditions. This week it announced its first big discovery: the genetic and molecular basis of a previously unexplained condition that causes painful calcification of the arteries.

Currently, only nine individuals are known to have the disorder, dubbed "arterial calcification due to CD73 deficiency". Researchers analysed the DNA of five affected siblings and found that they all had mutations of the NT5E gene, which codes for the CD73 enzyme that produces adenosine - a molecule that helps prevent arteries from calcifying (The New England Journal of Medicine, vol 364, p 432). The findings offer targets for a treatment. The discovery is impressive for its speed and technical prowess, says William Gahl, director of the UDP. "The role of adenosine was not known before."

<http://www.physorg.com/news/2011-02-hugs-tell-us-much-about.html>

### **Hugs tell us much about shared experiences**

***(PhysOrg.com) - In the run-up to Valentine's Day, couples the world over will be thinking about how they can convey their love to their partner in a meaningful and lasting manner.***

One of the most obvious ways a person can share their feelings is through physical gestures such as hugs which, according to new research from the University of Dundee, last an average of three seconds.

The study into the post-competition embraces of Olympic athletes, which was published in the latest edition of the Journal of Ethology, was led by Dr Emese Nagy, from the University's School of Psychology.

This research confirmed that a hug lasts about as long as many other human actions, and supports a hypothesis that we go through life perceiving the present in a series of about three-second windows.

Cross-cultural studies over the past century have shown that people tend to operate in these bursts. Goodbye waves, musical phrases, and infants' bouts of babbling and gesturing all last about three seconds.

"What we have is very broad research showing that we experience the world in these three-second time frames," Dr Nagy explained.

"Many basic physiological events, such as taking a breath and exhaling, last about 2-3 seconds each. When music and dance and other things are broken down we can see that these actually consist of singular movements bound together. This has been referred to as the "feeling of nowness" and we began looking at how long these moments last and whether we can objectively measure their duration."

"The memories of these moments become our personal stories, but they are our own individual experiences - what we wanted to do with this research was explore whether we ever share these movements which are so unique and subjective. We wanted this study to go a step further and see whether these moments can be experienced by two people at the same time - if we can ever share our internal reality - and whether these moments ascribe to the three-second hypothesis."

Dr Nagy, a keen gymnastics fan, was struck by how the behaviour of athletes encapsulated strong emotions. She hit upon the idea of analysing the embraces of gymnasts at the Beijing Olympics to see whether their hugs, either celebratory or consoling, fitted with the previously identified pattern. Most of the existing three-second research had been done on individuals, and she wondered whether the pattern would hold for an experience shared between two people, especially one as intimate and emotionally charged as an embrace.

Dr Nagy then conducted a frame-by-frame analysis of video recordings of the Olympic finals in 21 sports, among them badminton, wrestling, and swimming. She had an independent observer time 188 hugs between athletes from 32 nations and their coaches, teammates, and rivals. Regardless of the gender or national origin of the athletes and their partners, the hugs lasted about three seconds on average. The results reinforce the idea that intervals of about three seconds are basic temporal units of life that define our perception of the present moment.



Dr Nagy continued, "I was watching the Olympics and thought that this was the perfect example illustrating how people experiencing these feelings want to share them with other people. It was a shared moment which we could clearly mark the beginning and end of. The other people may be similarly emotionally charged, such as team mates and coaches, whereas others may be competitors or more dispassionate observers. The interesting thing is that, regardless of culture, nationality or gender, they all shared the moment through a hug whether they were expressing happiness, comforting, or being comforted."

"Our research illustrated that these feelings can be transmitted to another person to make the movement a shared experience. These moments may increase the likelihood of sharing further experiences, synchronization of further movements, and ultimately, could lead to the feeling of "togetherness" between people."

*Provided by University of Dundee*

<http://news.sciencemag.org/scienceinsider/2011/02/interior-department-inks-scienti.html>

### **Interior Department Inks Scientific Integrity Policy**

**by Erik Stokstad on 1 February 2011, 5:59 PM**

***The Department of the Interior (DOI) has finalized its policy on scientific integrity, creating code of conduct and procedures for investigation, as well as designating an official in charge.***

The policy was warmly welcomed by science organizations and advocates. But some details remain murky, such as whether whistleblowers will be protected in all situations. The policy is also vague about how it will ensure the transparency of science in decision-making. Not long after taking office in 2009, President Barack Obama called for a strategy to ensure scientific integrity at federal agencies and asked the Office of Science and Technology Policy to come up with recommendations. Even before OSTP finished its guidance, DOI had released a draft policy. Today the agency published its official policy.

All employees from scientists to policy makers, the departmental manual now declares, should "act in the interest of the advancement of science and scholarship for sound decision making, by using the most appropriate, best available, high quality scientific and scholarly data and information." There's also list of further requirements for scientists. (Note to peer-reviewers: "professional jealousy" is now verboten.)

The policy clearly spells out what employees should do if they suspect scientific misconduct and how it will be investigated. Ralph Morgenweck, a senior science advisor at the department's Fish and Wildlife Service (FWS), was appointed as the chief scientific integrity officer who will review allegations of misconduct.

Jeff Ruch of the group Public Employees for Environmental Responsibility says the policy is big step in the right direction and praises DOI for being the first agency to formalize a new policy. "We're glad they're finally venturing to this level" of detail, he says. (PEER's analysis is here.) But Ruch says the agency should have specifically stated that it will protect whistleblowing about scientific misconduct. The Whistleblower Protection Act covers federal employees who report crime, gross mismanagement or danger - but not necessarily scientific misconduct, Ruch says. According an agency official: "Scientists are fully protected under Federal Whistleblower protections and this policy acknowledges those protections."

Ruch also wishes that the policy explicitly stated the rights of agency scientists to publish their findings (as is FWS's) and to communicate with the media, as opposed to simply saying they "may" do that. The policy also lacks detail about how it will ensure transparency of scientific information used to make decisions. There are no timelines for releasing information mentioned, for example. DOI responds that "the addition of the scientific integrity officers as outlined in this new policy strengthens Interior's commitment to transparent, science-based decision-making."

<http://www.washingtonpost.com/wp-dyn/content/article/2011/02/01/AR2011020100169.html>

### **Ship wreck reveals ancient secrets of medicine**

**By Adrian Higgins Washington Post Staff Writer**

***It has been more than 2,000 years since a Roman merchant ship foundered off the west coast of the Italian peninsula and almost 40 years since the wreck was discovered. Now, the DNA trapped in medicines found aboard the ship is yielding secrets of health care in the ancient world.***

Samples from two tablets analyzed at the Smithsonian's Center for Conservation and Evolutionary Genetics reveal a dried concoction of about a dozen medicinal herbs, including celery, alfalfa and wild onion, bound together with clay and zinc. The tablets may have been used externally to treat skin conditions or dissolved in water or wine and taken for intestinal ailments such as dysentery, speculates Alain Touwaide, historian of sciences in the Department of Botany at the Smithsonian's National Museum of Natural History.

The DNA tests confirm that medicines written about in ancient texts were actually used, said Touwaide, who with his wife and research partner, Emanuela Appetiti, obtained the tablets from the Italian Department of Antiquities in 2004.

Archaeologists have found older artifacts in Egypt and China, vessels for wines that contained herbal additives. Touwaide, however, says the shipwreck tablets are the first remains of ancient pharmaceuticals to be found and also the first to be successfully analyzed with advanced DNA sequencing techniques. Preserved inside small tin boxes, the tablets are gray-green solid disks about an inch across and one-third of an inch thick.

"Extracting the DNA and sequencing it was not an easy task," Touwaide said.

The analyses were conducted intermittently over four years, the last in October, by Smithsonian geneticist Robert Fleischer, who said that the results are preliminary and that more testing is in the works. "I didn't expect it to work at all," said Fleischer. "They're very old. I had assumed everything had degraded, but they were in pretty remarkable condition. You could still see plant fibers." The ingredients also include radish or cabbage, wild carrot or a relative, yarrow, jack bean and a hibiscus species. Fleischer found smaller genetic traces that may be a carrot relative named angelica, as well as willow, aster, the common bean and nasturtium.

### **A tramp freighter?**

The ship was about 50 feet long, dates to around 130 B.C. and went down in the Gulf of Baratti off the coast of Tuscany. It was discovered in 1974 by members of the Italian Experimental Center for Underwater Archaeology, but its contents were not surveyed and excavated until the 1980s. Touwaide and Appetiti received the tablet fragments under an agreement between the Smithsonian and the Archaeological Department of Tuscany.

Divers retrieved several tin containers, 136 vials made of boxwood, a locker and medical tools. The large number of vials suggests that the medicines were being shipped rather than being used by the ship's doctor. "It might be both," said Touwaide. "There might have been a physician on board; there might have been a medical cargo." Among the recovered objects are glass from Syria, a Cypriot pitcher and lamps from Asia Minor, suggesting the vessel may have been a tramp freighter plying the ports of the entire Mediterranean.

That may be a false assumption, according to Cemal Pulak, vice president of Texas A&M University's Institute of Nautical Archaeology, who said the items might have been stored in a port and placed on the ship all at once, or salvaged from another wreck. Pulak, who is not involved with the Tuscan wreck, has excavated and studied eastern Mediterranean shipwrecks that date to the Bronze Age.

He said the warm waters of the Mediterranean are rich in shipwreck-eating microbes, and although hundreds of ancient shipwrecks have been recorded in the Mediterranean, to have any organic matter survive through the centuries "is a rare situation, and even rarer the circumstances where DNA is still viable."

### **Adding credence to texts**

Touwaide said the medicines discovered on the wreck support his theory that though apothecaries had access to hundreds of medicinal plants, they purposefully limited their palette to a few herbs but used them in different formulas to treat a range of ailments. "You're in a better position if you reduce the number of substances. If you have substances that are easy to find and native to your region, you can always come up with a remedy," said Touwaide.

The Hippocratic Collection, a series of ancient Greek texts attributed to Hippocrates, who is often called the father of Western medicine, refers to 380 medicinal herbs useful for a variety of ailments, Touwaide said, but he added that ancient Greek healers relied mainly on just 45 plants. Among the herbs found in the two tablets was wild carrot, for instance, which had been identified by the 1st-century Greek pharmacologist Dioscorides as a diuretic that was used to treat colic, wounds and poisonous bites.

"Nobody really knew anything about how the body worked or the chemical properties of these substances," said Mark J. Schiefsky, a professor of classics at Harvard University. "It was a kind of folk medicine that did have a basis in experience." He said the find helps bridge the gap between historical theory and practice.

Touwaide said he was heartened by the apparent absence of opium, incense or myrrh in the tablets - ingredients that would have diminished the validity of the other herbs as effective medicines. Opiates would have overpowered the other medicines, he said, and the tree resins would have shifted the tablets into the realm of magic potion. On the contrary, the tablets now lend a greater credence to the medical texts of Dioscorides and his Roman successor, Galen. "The identification of the components shows that the texts were put into practice, or we can turn it upside down and say that the texts recorded the practice," he said.

Touwaide said that as a result of the discovery, he is studying with more confidence Galen's references to using broccoli in the treatment of intestinal cancer. Broccoli is closely related to cabbage.

Fleischer presented the results of his tests at a gathering of biomolecular archaeologists in Copenhagen in September. The Smithsonian team hopes to get more material in May as part of further testing before writing a scientific paper about the findings. They would like to identify a few organic substances that have so far proved to be unidentifiable. They also want to retest for sunflower, which showed up in the results. Botanists view the

sunflower as a New World plant unknown in ancient Rome and Greece. If its presence on the wreck, the Relitto del Pozzino, is confirmed, "it would be a big discovery," said Touwaide.

Fleischer, however, is leaning more toward sample contamination as the cause. The reagents used to sequence the DNA may have been the source of the sunflower trace, he said.

[http://www.eurekalert.org/pub\\_releases/2011-02/asoh-eio020311.php](http://www.eurekalert.org/pub_releases/2011-02/asoh-eio020311.php)

### **Early infusion of donor T cells prevents graft versus host disease in blood cancer patients**

**WASHINGTON – For blood cancer patients at high risk of relapse, hematopoietic stem cell transplantation (HSCT), the transplantation of blood-forming stem cells, is one of best options for treatment and a potential cure.**

Unfortunately, the most common complication of HSCT is graft-versus-host disease (GVHD), a serious and often deadly post-transplant complication that occurs when the newly transplanted donor cells recognize the recipient's own cells as foreign and react by attacking the cells in the patient's body. A study published today in *Blood*, the Journal of the American Society of Hematology, highlights updated results for a potential new strategy for preventing GVHD and promoting the patient's immune system recovery after transplant.

Patients who do not have a compatible donor in the family or in donor registries must rely on a transplant from alternative sources, such as a partially matched donor, as their only hope for cure. To ensure the success of transplants from partially matched donors, the donated stem cells must be treated before they are transplanted into the patient. This treatment depletes the donor's T cells, which are critical for promoting immune recovery after transplant but can also trigger severe and potentially fatal GVHD. Therefore, managing the dual function of T cells is critical before and after the transplant procedure.

In a trial conducted at the University of Perugia in Italy by a group that has pioneered the use of partially matched donors, researchers explored the use of a population of T cells called regulatory T cells (Tregs) that control immune reactions. Regulatory T cells have been widely studied in animal models and have been shown to promote the acceptance of organ grafts and control abnormal immune reactions associated with GVHD. They have not yet been tested in humans prior to this study, which enrolled 22 patients with acute myeloid leukemia (AML), five patients with acute lymphoid leukemia (ALL), and one patient with high-grade non-Hodgkin lymphoma. Four days before HSCT, the 28 patients were infused with donor Tregs, and on the day of the transplant, they were infused with normal T cells in an effort to simultaneously prevent GVHD and promote immune system recovery.

"Our aim was to determine if patient outcomes could be improved if Tregs were introduced early in the transplantation process," said senior study author Massimo F. Martelli, MD, Full Professor and Head of the Umbria Region Bone Marrow Transplantation Program at the University of Perugia.

Results of the study revealed that 26 patients achieved full-donor engraftment, meaning that all of the transplanted donor cells were able to reproduce into new, cancer-free cells. Only two of the 26 patients that were evaluated developed acute GVHD, and at median follow-up of 11.2 months none of the patients had developed chronic GVHD. The immune system of these patients was restored to normal levels, better than other patients who had not received the T cell infusions. There were also fewer episodes of the reactivation of Cytomegalovirus (CMV), a common virus known as a major cause of morbidity and mortality after HSCT due to a weakened immune system, and no patient developed CMV disease. Furthermore, early Treg infusion was not associated with an increased incidence of leukemia relapse; only one relapse had occurred at median follow-up of 12 months in a patient with AML. One patient died from adenoviral infection and GVHD and one died from GVHD; at median follow-up of 12 months, 12 patients (46.1 percent) were alive and disease-free.

"This is an update of the first study in humans that demonstrates that regulatory T cell-based therapy ensures that hematopoietic stem cell transplant is successful, without triggering GVHD, by reconstituting the patient's immune system faster than standard transplant methods," said Mauro Di Ianni, MD, senior study co-author and Researcher at the Hematology and Clinical Immunology Section at the University of Perugia.

[http://www.eurekalert.org/pub\\_releases/2011-02/drnl-os020311.php](http://www.eurekalert.org/pub_releases/2011-02/drnl-os020311.php)

### **'Tall order' sunlight-to-hydrogen system works, neutron analysis confirms**

**OAK RIDGE, Tenn. - Researchers at the Department of Energy's Oak Ridge National Laboratory have developed a biohybrid photoconversion system - based on the interaction of photosynthetic plant proteins with synthetic polymers - that can convert visible light into hydrogen fuel.**

Photosynthesis, the natural process carried out by plants, algae and some bacterial species, converts sunlight energy into chemical energy and sustains much of the life on earth. Researchers have long sought inspiration from photosynthesis to develop new materials to harness the sun's energy for electricity and fuel production.

In a step toward synthetic solar conversion systems, the ORNL researchers have demonstrated and confirmed with small-angle neutron scattering analysis that light harvesting complex II (LHC-II) proteins can self-assemble with polymers into a synthetic membrane structure and produce hydrogen. The researchers envision energy-producing photoconversion systems similar to photovoltaic cells that generate hydrogen fuel, comparable to the way plants and other photosynthetic organisms convert light to energy.

"Making a self-repairing synthetic photoconversion system is a pretty tall order. The ability to control structure and order in these materials for self-repair is of interest because, as the system degrades, it loses its effectiveness," ORNL researcher Hugh O'Neill, of the lab's Center for Structural Molecular Biology, said.

"This is the first example of a protein altering the phase behavior of a synthetic polymer that we have found in the literature. This finding could be exploited for the introduction of self-repair mechanisms in future solar conversion systems," he said.

Small angle neutron scattering analysis performed at ORNL's High Flux Isotope Reactor (HFIR) showed that the LHC-II, when introduced into a liquid environment that contained polymers, interacted with polymers to form lamellar sheets similar to those found in natural photosynthetic membranes.

The ability of LHC-II to force the assembly of structural polymers into an ordered, layered state - instead of languishing in an ineffectual mush - could make possible the development of biohybrid photoconversion systems. These systems would consist of high surface area, light-collecting panes that use the proteins combined with a catalyst such as platinum to convert the sunlight into hydrogen, which could be used for fuel.

The research builds on previous ORNL investigations into the energy-conversion capabilities of platinized photosystem I complexes - and how synthetic systems based on plant biochemistry can become part of the solution to the global energy challenge.

"We're building on the photosynthesis research to explore the development of self-assembly in biohybrid systems. The neutron studies give us direct evidence that this is occurring," O'Neill said.

The researchers confirmed the proteins' structural behavior through analysis with HFIR's Bio-SANS, a small-angle neutron scattering instrument specifically designed for analysis of biomolecular materials.

"Cold source" neutrons, in which energy is removed by passing them through cryogenically chilled hydrogen, are ideal for studying the molecular structures of biological tissue and polymers.

The LHC-II protein for the experiment was derived from a simple source: spinach procured from a local produce section, then processed to separate the LHC-II proteins from other cellular components. Eventually, the protein could be synthetically produced and optimized to respond to light.

O'Neill said the primary role of the LHC-II protein is as a solar collector, absorbing sunlight and transferring it to the photosynthetic reaction centers, maximizing their output. "However, this study shows that LHC-II can also carry out electron transfer reactions, a role not known to occur in vivo," he said.

The research team, which came from various laboratory organizations including its Chemical Sciences Division, Neutron Scattering Sciences Division, the Center for Structural Molecular Biology and the Center for Nanophase Materials Sciences, consisted of O'Neill, William T. Heller, and Kunlun Hong, all of ORNL; Dimitry Smolensky of the University of Tennessee; and Mateus Cardoso, a former postdoctoral researcher at ORNL now of the Laboratio Nacional de Luz Sincrotron in Brazil. "That's one of the nice things about working at a national laboratory. Expertise is available from a variety of organizations," O'Neill said.

*The work, published in the journal Energy & Environmental Science, was supported with Laboratory-Directed Research and Development funding. HFIR is supported by the DOE Office of Science.*

*ORNL is managed by UT-Battelle for the Department of Energy's Office of Science.*

<http://www.newscientist.com/article/dn20083-after-the-birds-vanish-plants-are-next-to-go.html>

### **After the birds vanish, plants are next to go**

**\* 19:00 03 February 2011 by Wendy Zukerman**

#### ***The first evidence that the loss of a bird species could damage the prospects of particular plants has heightened fears for vulnerable plants around the world.***

Many plants rely on birds to pollinate them and disperse their seeds, so it seems reasonable to assume that if the bird population falls, this will have a knock-on effect on plant species. Now the effect has been seen in a shrub, following the extinction of two birds – the bellbird (*Anthornis melanura*) and stitchbird (*Notiomystis cincta*) – on New Zealand's North Island after rats were introduced there in the 1870s.

The flowering shrub *Rhabdothamnus solandri* relies on these two birds, as well as two other species, for pollination. Dave Kelly from the University of Canterbury in Christchurch, New Zealand, and colleagues examined how the plant fared on the North Island compared with how well it was doing on nature reserves on three smaller islands where these birds survive.

## Helping hand

The team hand-pollinated flowers on 79 plants throughout the North Island and the three island sanctuaries, and compared their fruit production with untouched flowers in these locations.

Around 70 per cent of the hand-pollinated flowers produced fruit on the North Island and the smaller islands. Without this intervention, only 22 per cent of the flowers on the North Island produced fruit, compared to 58 per cent on the island sanctuaries. North Island fruits were also smaller and, on average, produced 84 per cent less seed than fruits on the smaller islands – a clear sign that their seeds are not getting fully pollinated.

Reduced seed production is already affecting the *Rhabdothamnus solandri* population: there are fewer than half as many young plants per adult plant on the North Island compared with the smaller islands.

### There's still time...

Kelly is confident that the lack of pollinating birds is to blame. Field observations showed evidence of birds visiting up to 80 per cent of the flowers on the islands where the bellbird and stitchbird still thrive, but only a quarter of the flowers where these birds had disappeared. "Plant extinctions tend to be slower than animals, because plants live longer," says Kelly. "We have time to do something about it," he says, such as repopulating the North Island with stitchbirds and bellbirds. He estimates that *Rhabdothamnus solandri* can live for over 150 years.

"This is really compelling," says Martine Maron, a bird ecologist at the University of Queensland in Brisbane, Australia. Since birds are responsible for pollinating a large proportion of flowering plants, "the problem is likely to be occurring all around the world", she says. "It is not just about losing a species from the face of the Earth," Maron adds. "Losing key species from local areas can result in ecosystem collapse."

Journal reference: *Science*, DOI: 10.1126/science.1199092

<http://www.bbc.co.uk/news/science-environment-12356835>

## Amazon drought 'severe' in 2010, raising warming fears

By Richard Black Environment correspondent, BBC News

### Last year's drought in the Amazon raises concerns about the region's capacity to continue absorbing carbon dioxide, scientists say.

Researchers report in the journal *Science* that the 2010 drought was more widespread than in 2005 - the last big one - with more trees probably lost. The 2005 drought had been termed a "one in a century" event.

In drought years, the Amazon region changes from being a net absorber of carbon dioxide into a net emitter.

The scientists, from the UK and Brazil, suggest this is further evidence of the Amazon's vulnerability to rising global temperatures. They also suggest the days of the Amazon forest curbing the impact of rising greenhouse gas emissions may be coming to an end.

The 2010 drought saw the Amazon River at its lowest levels for half a century, with several tributaries completely dry and more than 20 municipalities declaring a state of emergency.

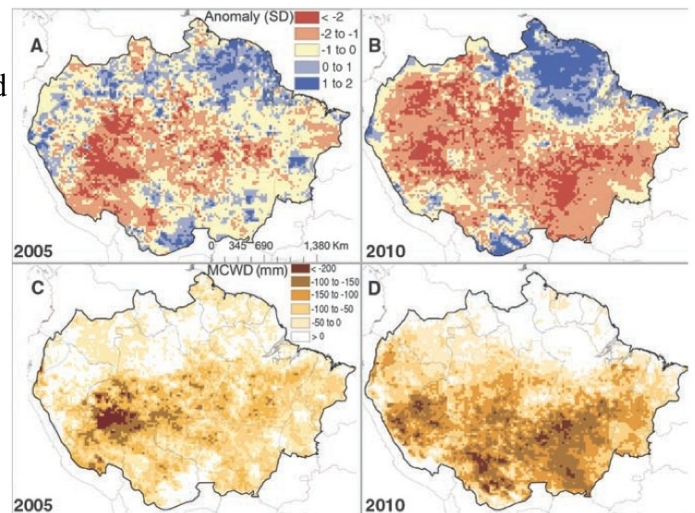
Research leader Simon Lewis, from the University of Leeds, is the scientist who gained an apology from the Sunday Times newspaper last year over the so-called "AmazonGate" affair. "It's difficult to detect patterns from just two observed droughts, but to have them close together is concerning," he told BBC News.

Both droughts were associated with unusually warm seas in the Atlantic Ocean off the Brazilian coast.

"If that turns out to be driven by escalating greenhouse gas concentrations in the atmosphere, it could imply that we'll see more drought years in the near future," said Dr Lewis. "If events like this do happen more often, the Amazon rainforest would reach a point where it shifts from being a valuable carbon sink slowing climate change to a major source of greenhouse gases."

Some computer models of climate change - in particular, the one developed at the UK's Hadley Centre - project more droughts across the region as the planet warms, and a diminishing capacity to absorb CO<sub>2</sub>.

There are several ways in which warming can turn greenhouse gas-absorbing forests into emitters. In the Amazon, the principal mechanism is simply that trees die and then rot; in addition, those trees are then not available to absorb CO<sub>2</sub> from the air.



## Eye in the sky

For this research, scientists used data from the Tropical Rainfall Measuring Mission (TRMM), a US/Japanese satellite that monitors rainfall in a belt extending either side of the Equator. Its observation showed that whereas the 2005 drought covered an area of nearly two million sq km, in 2010 it stretched for three million sq km.

Following the 2005 drought, scientists were able to study the impact on trees and work out the relationship between the rainfall loss and the release of carbon.

In an average year, the basin absorbs about 1.5 billion tonnes of CO<sub>2</sub> from the atmosphere. By contrast, the impact of the 2005 drought, spread over a number of years, was calculated as a release of five billion tonnes.

The new paper calculates the figure for 2010 as about eight billion tonnes, as much as the annual emissions of China and Russia combined; but this, the researchers acknowledge, is a first estimate.

"It could be that many of the susceptible trees were killed off in 2005, which would reduce the number killed last year," said Paulo Brando from the Amazon Institute of Environmental Research (IPAM) in Belem, Brazil.

"On the other hand, the first drought may have weakened a large number of trees, so increasing the number dying in the 2010 dry season."

Leeds University is part of a research group that maintains about 130 land stations across the Amazon region.

If funds are forthcoming, the team will visit them all in the coming months to gather first-hand data on tree deaths. This should provide for a more accurate estimate of the 2010 drought's contribution to global emissions.

## Closing the gate

The likely fate of the Amazon under climate change came under focus early last year when, as one of a series of attacks on the Intergovernmental Panel on Climate Change (IPCC), the Sunday Times newspaper accused the panel of having included an unsubstantiated claim that up to 40% of the forest could be affected by climate change in future. It used quotes from Dr Lewis in support of its claim. In fact, Dr Lewis was concerned about the region's vulnerability and had sent the newspaper a sheaf of scientific papers to back the case.

He told the newspaper that the IPCC had sourced its statement to a report from environmental group WWF, when it should have referenced the scientific papers WWF had used in its report. "In fact, the IPCC's Amazon statement is supported by peer-reviewed scientific evidence," the Sunday Times acknowledged in its apology.

Commenting on that so-called "AmazonGate" episode from the perspective of the new research, Dr Lewis noted: "The notion that the Amazon is potentially very vulnerable to droughts linked to climate change was reasonable and defensible at the time, and is consistent with the new findings.

"If greenhouse gas emissions contribute to Amazon droughts that in turn cause forests to release carbon, this feedback loop would be extremely concerning. "Put more starkly, current emissions pathways risk playing Russian roulette with the world's largest rainforest."

<http://www.physorg.com/news/2011-02-ohsu-complex-heart-problems-open-heart.html>

## **OHSU fixes complex heart problems without open-heart surgery**

***The pediatric cardiac team at Oregon Health & Science University Doernbecher Children's Hospital is the first in the region and one of a handful in the nation to implant a pulmonary heart valve without open-heart surgery.***

To date, four patients have received the landmark valve in the OHSU Pediatric and Adult Congenital Cardiac Catheterization Lab. All reported immediate improvement in their energy level and stamina.

The device, called the Medtronic Melody® Transcatheter Pulmonary Valve, recently was approved by the Food and Drug Administration. The valve is used to replace a narrow or leaky pulmonary valve "conduit" - a tube connecting the heart to the lungs - in children and adults who previously have undergone surgery to correct a congenital heart defect. Until now, pulmonary valve replacements have required open-heart surgery.

The Melody valve is inserted into a tiny opening in the leg and guided by a catheter through blood vessels into the heart. Once the valve is correctly positioned, a balloon on the end of the catheter is inflated, delivering the valve and immediately correcting blood flow.

"Children born with blocked or leaky heart valves can undergo as many as four open-heart surgeries before reaching adulthood to replace conduits that have worn out or that they've outgrown, and each time the risk of surgery goes up," said Grant Burch, M.D., director of the OHSU Pediatric and Adult Congenital Cardiac Catheterization Lab and associate professor of pediatric cardiology at OHSU Doernbecher Children's Hospital. "The Melody extends the useful life of an implanted valve conduit and is very likely to reduce the number of open-heart operations a patient might require over a lifetime."

"This device is not going to abolish the need for open-heart surgery, but it does provide a safe and effective alternative to surgery for many children and young adults with congenital heart disease," explained Burch.

"The remarkable thing about this procedure is that the valve is placed into the beating heart through a vein in the patient's leg. After the procedure, patients spend a night on the hospital ward and are discharged home the following morning," said Laurie Armsby, M.D., associate professor of pediatric cardiology at OHSU Doernbecher and Burch's partner in the OHSU Pediatric and Adult Congenital Cardiac Catheterization Lab. "This device brings us closer to the goal of providing children less invasive alternatives to surgery for the treatment of congenital heart disease."

More than 1,700 patients have been implanted worldwide since the valve was approved for commercial use in Europe in 2006. According to the FDA, an estimated 1,000 U.S. children and adults with congenital heart disease will qualify for the new valve annually. Drs. Burch and Armsby are the only pediatric cardiologists in Oregon with advanced training in interventional cardiology. Together they perform more than 300 cardiac catheterizations in newborns, children, and adults with congenital heart disease each year.

The FDA approved the Melody valve under the Humanitarian Device Exemption provision, which allows for the use of devices determined to be safe and whose benefits to health outweigh the risk of injury or illness. A Humanitarian Use Device (HUD) is intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year. The exemption is only given when there are no comparable devices available to treat or diagnose the disease or condition. *Provided by Oregon Health & Science University*

<http://www.bbc.co.uk/news/health-12354032>

### **Diabetes and virus link confirmed**

#### ***Children with Type 1 diabetes are nearly 10 times as likely to also have a viral infection than healthy children, Australian research suggests.***

Childhood diabetes has been linked to enteroviruses, which can lead to cold, flu and even meningitis. However the review of 26 existing studies by a group in Australia, [\*published in the BMJ\*](#), does not prove that the virus causes diabetes. Diabetes UK said more research was needed to pinpoint the cause of Type 1.

The illness typically appears in childhood, when the pancreas stops producing the hormone insulin and the body cannot control the level of sugar in the blood.

#### **More common**

The number of cases has been increasing, without explanation, across the globe. There is a genetic factor to Type 1 diabetes but this does not explain the rise, so scientists are searching for environmental factors.

One of these is thought to be the enterovirus, yet previous studies on the virus have been inconsistent.

Researchers at the University of New South Wales and the Institute of Endocrinology and Diabetes in Sydney combined the research of several groups to provide a more definitive answer.

They reviewed 26 sets of research involving 4,448 patients and concluded: "The association between enterovirus infection, detected with molecular methods, and diabetes was strong, with almost 10 times the odds of enterovirus infection in children at diagnosis of Type 1 diabetes.

Dr Jonathan Levy, consultant diabetologist at the Oxford Centre for Diabetes, Endocrinology and Metabolism, said: "It looks to be a very well conducted study that seems to nail the association very dramatically, especially in the newly diagnosed."

#### **The root of the problem**

One of the issues with this type of research is that it is hard to prove what causes what. Enterovirus could cause diabetes, or diabetes could make you more susceptible to enterovirus - or something else, such as genetic makeup, could make you more likely to get both.

The authors acknowledge more studies need to take place. Dr Iain Frame, director of research at Diabetes UK, said: "Many factors have been reported as being associated with Type 1 diabetes but that is not the same as causing Type 1 diabetes and this report based on looking at a number of previous studies does not bring us much closer to pinpointing the causes of Type 1 diabetes. We do, however, welcome any new analysis that brings about a better understanding of the involvement of certain viruses on the insulin-producing cells in the pancreas. "It may well give us another piece of the jigsaw in working towards a better understanding of the causes of Type 1 diabetes which should in turn lead to new prevention strategies."

Dr Alan Foulis, who has been researching the link between diabetes and viruses at Glasgow Royal Infirmary, said: "There's evidence of enterovirus involvement, but there are too many different enteroviruses, hundreds of them. What researchers are trying to do is pool resources across Europe to find out which enteroviruses could be associated with Type 1, which a vaccine manufacturer would need to know to pinpoint the exact one to target."

## **HIV-like infection banished from mice**

\* 11:29 04 February 2011 by Wendy Zukerman

***For the first time, an HIV-like infection has been cleared from an animal without the use of antiviral drugs. The infection was eliminated from mice using a human protein that peps up immune cells.***

Marc Pellegrini from the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia, and colleagues infected mice with lymphocytic choriomeningitis virus (LCMV), which causes a chronic infection that spreads throughout the body. "The virus overwhelms mice, mimicking the massive viral loads associated with HIV infection in humans," says Pellegrini.

Eight days after infection, some of the mice were injected with human interleukin-7 (IL-7) – a chemical messenger that plays a role in the development of immune cells – once a day for three weeks. The others received a placebo instead. "Usually mice never clear this virus," says Pellegrini. But 30 days later, those given treatment had cleared most of the infection and removed all of it by 60 days.

### **Overactive response**

The explanation seems to lie in a protein called SOCS3, which blocks the function of T-cells – a type of immune cell and therefore part of the body's system for fighting infection. At the beginning of an acute infection, SOCS3 becomes highly activated, suppressing the body's immune response. That sounds just the opposite of what you'd want. But it's a good thing because it stops T-cells being overzealous, which can cause damage to body tissue, says Pellegrini. It becomes a problem when the body is trying to fight an overwhelming infection like HIV, he says: then the immune system puts on the brakes too early and the infection persists. Blood tests taken throughout the experiment showed that IL-7 seemed to switch off the production of SOCS3, thereby ramping up the T-cell response.

### **Start and stop**

This explanation was confirmed when the team knocked out the SOCS3 gene in a separate group of mice and infected them with LCMV. Immune cell numbers in these mice skyrocketed – T-cells increased sixfold compared with normal mice. But knocking out SOCS3 showed the dangers of taking the immune brakes off. "Initially the mice mounted a robust immune response, but then it got out of hand," says Pellegrini. The mice developed mass inflammation and increased incidences of autoimmune diseases. However, because IL-7 only affects T-cells, and not other types of immune cell, the researchers suggest that drugs could be developed that turn off SOCS3 for very short periods to reinvigorate T-cells without causing damage to the body.

Sharon Lewin at the Burnet Institute in Melbourne says the finding that IL-7 can clear the virus without the help of antiviral drugs is very interesting. Viruses like HIV use the host's cells to replicate, which makes it difficult to design antivirals that stop the virus without harming healthy cells.

"[Stopping a virus] without antivirals is something we haven't seen before," she says.

*Journal reference: Cell, DOI: 10.1016/j.cell.2011.01.011*

[http://www.eurekalert.org/pub\\_releases/2011-02/vu-doj020411.php](http://www.eurekalert.org/pub_releases/2011-02/vu-doj020411.php)

## **Discovery of jumping gene cluster tangles tree of life**

***Since the days of Darwin, the "tree of life" has been the preeminent metaphor for the process of evolution, reflecting the gradual branching and changing of individual species.***

The discovery that a large cluster of genes appears to have jumped directly from one species of fungus to another, however, significantly strengthens the argument that a different metaphor, such as a mosaic, may be more appropriate. "The fungi are telling us something important about evolution ... something we didn't know," said Antonis Rokas, assistant professor of biological sciences at Vanderbilt. He and research associate Jason Slot reported their discovery in the Jan. 25 issue of the journal *Current Biology*.

Rokas and Slot discovered that millions of years ago, a cluster of 23 genes jumped from one strain of mold commonly found on starchy foods like bread and potatoes, *Aspergillus*, to another strain of mold that lives in herbivore dung and specializes in breaking down plant fibers, *Podospora*.

The findings came as a major surprise, as there are only a handful of cases in recent evolutionary history where this type of gene transfer between organisms, known as horizontal gene transfer, has been reported in complex cells like those found in plants, animals and fungi. "Because most people didn't believe that such large gene clusters could be transferred horizontally, they haven't looked for them and they haven't been found," Rokas said. Rokas and Slot detected the unprecedented gene cluster transfer during a detailed comparison of the entire genomes of nearly 100 species of fungi. The primary goal of their research is to identify the most reliable methods for determining the evolutionary relationships of species of all kinds. In the course of their analysis, they discovered the 23-gene capture. The jumping gene cluster codes for a toxic compound called



sterigmatocystin. Cells produce this type of compound to attack competing organisms or to protect themselves from attacks. As a result, these types of compounds are the source of a number of important drugs, like penicillin and cyclosporin, as well as a number of natural poisons.

"Fungi produce an astonishing variety of drugs and poisons. Our discovery that one of the largest gene clusters responsible for making such a poison moved intact between species suggests that horizontal transfers of wholesale pathways may have contributed significantly to the generation of this diversity," Rokas said.

In the past, evolutionary research has focused on the passage of genes from parent to child, known as vertical gene transfer. This process, acted out over the eons of geological time, gives rise to the branching structure of the tree of life.

Since the 1980's, however, evolutionary scientists have become increasingly aware that horizontal or lateral gene transfer also plays a major role in evolution. In vertical gene transfer, all the genetic material in each new species come from a single ancestral species. In horizontal gene transfer, by contrast, species that receive bits of genetic material from its neighbors are directly related to a number of often unrelated species. Horizontal gene transfer was first discovered in bacteria, and has been recognized as largely responsible for the problem of drug resistance. If one bacterium evolves a method for surviving a drug, this ability can spread rapidly to other unrelated microorganisms via horizontal gene transfer, substantially reducing the drug's effectiveness.

Though researchers now generally agree that horizontal gene transfer is relatively common among simple organisms like bacteria, they have continued to assume that it remained relatively rare among complex organisms like plants and animals. "The thinking has been that there is very little horizontal gene transfer among plants and animals except for a few big, ancient events and maybe the occasional transfer of a single gene here or there," Slot said. "Our discovery suggests that the horizontal transfer of gene clusters may have been a big player not only in the evolution of bacteria but also in more complex organisms."

*This work was supported by funds provided by the Searle Scholars Program and the National Science Foundation.*

<http://www.newscientist.com/article/dn20088-woodpeckers-head-inspires-shock-absorbers.html>

## Woodpecker's head inspires shock absorbers

\* 15:16 04 February 2011 by Paul Marks

**When aircrash investigators of the future retrieve a flight recorder from the wreckage of a plane they may have the golden-fronted woodpecker, *Melanerpes aurifrons*, to thank for the survival of the flight data.**

The reason? A shock absorber inspired by the bird's ability to withstand severe deceleration. A woodpecker's head experiences decelerations of 1200g as it drums on a tree at up to 22 times per second. Humans are often left concussed if they experience 80 to 100g, so how the woodpecker avoids brain damage was unclear.

So Sang-Hee Yoon and Sungmin Park of the University of California, Berkeley, studied video and CT scans of the bird's head and neck and found that it has four structures that absorb mechanical shock.

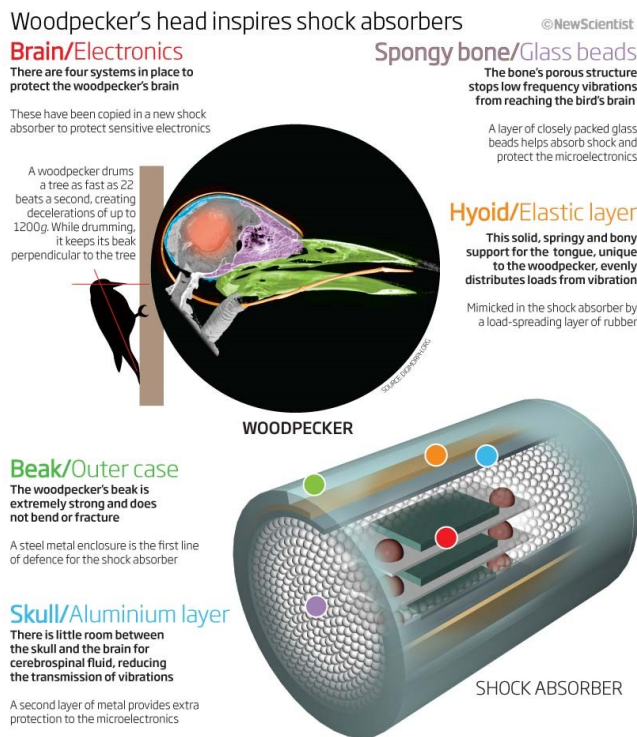
These are its hard-but-elastic beak; a sinewy, springy tongue-supporting structure that extends behind the skull called the hyoid; an area of spongy bone in its skull; and the way the skull and cerebrospinal fluid interact to suppress vibration.

### Artificial analogues

The researchers then set out to find artificial analogues for all these factors so they could build a mechanical shock absorbing system to protect microelectronics that works in a similar way.

To mimic the beak's deformation resistance, they use a cylindrical metal enclosure. The hyoid's ability to distribute mechanical loads is mimicked by a layer of rubber within that cylinder, and the skull/cerebrospinal fluid by an aluminium layer. The spongy bone's vibration resistance is mimicked by closely packed 1-millimetre-diameter glass spheres, in which the fragile circuit sits (see diagram).

To test their system, Yoon and Park placed it inside a bullet and used an airgun to fire it at an aluminium wall. They found their system protected the electronics ensconced within it against shocks of up to 60,000g. Today's flight recorders can withstand shocks of 1000g. "We now know how to prevent the fracture of



microdevices from mechanical shock," says Yoon. "An institute in Korea is now looking into some military applications for the technology."

### **Overcoming space debris**

As well as a possible role protecting flight recorder electronics, the shock absorber could also be used in "bunker-busting" bombs, as well as for protecting spacecraft from collisions with micrometeorites and space debris. It could also be used to protect electronics in cars.

"This study is a fascinating example of how nature develops highly advanced structures in combination to solve what at first seems to be an impossible challenge," says Kim Blackburn, an engineer at Cranfield University in the UK, which specialises in automotive impact studies.

"It may inform our thinking on regenerative dampers for vehicles, redirecting the energy into a form more easily recoverable than dumping it to heat," Blackburn adds. "Ultimately, we need to learn from the woodpecker to recover energy and not give the driver a headache."

Nick Fry, chief executive of Formula One team Mercedes GP Petronas based in Brackley, UK, says such ideas could feed into crash protection for drivers taking part in motorsport: "One big issue with Formula One is protecting the driver by getting them to decelerate in an accident situation in such a way that his internal organs and brain aren't turned to mush. We do that with clever design of composites, very sophisticated seatbelts and a head and neck restraint system," Fry says. "But this research might be something we can draw on in future – it could be very interesting." *Journal reference: Bioinspiration and Biomimetics, DOI: 10.1088/1748-3182/6/1/016003*  
<http://www.physorg.com/news/2011-02-guinea-worm-disease-smallpox.html>

### **Guinea worm disease may be second eliminated after smallpox**

***Health officials are poised to eradicate guinea worm disease, a plague that once afflicted millions and which would be just the second human disease wiped from the face of the earth, Donald Hopkins, vice president of health programs for The Carter Center, said Tuesday (Feb. 1).***

As recently as 1986, guinea worm disease affected 3.5 million people annually in 20 nations. After decades of effort, last year there were just 1,800 cases in four nations, the vast majority in Sudan. "We should be able to stop transmission of the disease by 2012 or soon thereafter. To that prospect, I say good riddance", Hopkins said.

Little known in the developed world, guinea worm disease is caused by drinking water containing a small crustacean infected by the worm larvae. Once inside a human host, the worm reproduces and grows. About a year after infection, female worms burrow under the skin and emerge from a painful blister, usually in the lower extremities. The resulting burning pain, which earned the parasite the moniker the "fiery serpent," causes those afflicted to immerse the blister in water, whereupon the female releases many larvae, repeating the cycle. Removing the worm, which can reach a meter in length, is a painful process that can take weeks, coiling the parasite around a stick until it fully emerges.

Hopkins described progress against the disease during the Yerby Diversity Lecture in Public Health at the Harvard School of Public Health (HSPH). He was introduced by HSPH Dean Julio Frenk.

The Carter Center has played a leading role in fighting the affliction, supporting national eradication programs and spearheading the international campaign. Hopkins said the surge in funding from major donors such as the Bill & Melinda Gates Foundation has also been critical. One remarkable facet of the effort, Hopkins said, is that it has been accomplished with no vaccine and no effective treatment for the disease. (Those infected develop no natural immunities, meaning they can be infected again and again.)

Instead, interventions included reaching out to communities afflicted by it, discussing how to ensure that drinking water is clean, and emphasizing the importance of keeping infected people out of the water. The effort exploded the myth that poor people won't play an active role in improving their own health, Hopkins said. The progress made would have been impossible without the cooperation of those afflicted. "Outsiders cannot save people suffering from problems such as these without the participation of the people suffering from the disease," Hopkins said.

Effectively utilizing key statistics was important in mobilizing decision makers in countries where guinea worm was still found. And, once progress was made in one place in eradicating the disease, other people wanted the same relief. "People will put up with a lot, until they see their neighbors are suffering no longer," Hopkins said. "Then they will demand action."

Because the worm's life cycle is dependent on a human host, there should be no natural reservoir for the parasite once it is eliminated in humans, and it should join smallpox - the last natural case of which was in 1977 - in the history books.

Eradicating the disease will bring many benefits, Hopkins said, not least of which will be releasing resources to other health priorities. Agricultural productivity is likely to increase, since farmers free from the disease will

be able to tend their fields. In addition, the lessons learned and the infrastructure created can inform and support future health efforts. Hopkins said many resources are still needed to battle other tropical diseases. A major international effort is already focused on malaria, and Hopkins said lymphatic filariasis, which causes elephantiasis, and measles are likely candidates for the next extermination campaign. "I am gratified but not satisfied. We can and should do more for our own sake and for that of others," Hopkins said.

Provided by Harvard University

<http://www.physorg.com/news/2011-02-japanese-stem-cell-award.html>

### **Japanese stem cell researcher wins top award**

**Japanese scientist Shinya Yamanaka was Friday honoured with a Spanish award worth 400,000 euros (\$544,000) for his pioneering work on cell reprogramming.**

Yamanaka won the BBVA Foundation Frontiers of Knowledge Award in Biomedicine, the foundation announced. The former orthopedic surgeon made his breakthrough discovery in 2006 when he succeeded in generating "induced pluripotent stem (iPS) cells", or those capable of growing into other tissues in the body.

Until Yamanaka proved differently, scientists believed that this could only be achieved with stem cells harvested from embryos, the foundation said in a statement. "The jury emphasised the exciting new vistas these cells open up for both basic and clinical research, with personalised therapies and more precisely targeted drugs," it added. "The possibility of working with iPS cells derived from patients themselves will avoid treating patients as guinea pigs. It will allow novel cell-based screening methods to be used to search for small molecule drugs to treat a wide range of diseases. "And, ultimately, it may also allow novel and even patient-specific cell-based treatments, in particular for degenerative disease."

Yamanaka said the idea of reversing the fate of already specialised cells, then a "no-can-do" in biology, came to him when studying the experiments that produced the first cloned frogs, in the 1970s, and Dolly the sheep in 1996, according to the foundation statement. "From their work I learned that we should be able to convert somatic cells back into their embryonic state. That is what inspired me to start my project," said Yamanaka, 48, the director of the Centre for iPS Cell Research and Application at Japan's Kyoto University.

The BBVA Foundation Frontiers of Knowledge Awards, established in 2008, recognise research and artistic creation in eight categories.

<http://www.physorg.com/news/2011-02-husband-giffords-flight-decision.html>

### **Husband: Giffords would be OK with flight decision**

**(AP) - The astronaut husband of wounded Rep. Gabrielle Giffords said his wife would be "very comfortable" with his decision to go back into space and he expects her to be at his launch in April.**

Space shuttle commander Mark Kelly wouldn't go into details about her condition during a news conference Friday, and deflected questions about how he knows she supports his choice to fly.

"I know her very well and she would be very comfortable with the decision that I made," he said. Kelly took a leave from training after Giffords was gunned down in Tucson, Ariz., on Jan. 8. NASA announced earlier Friday he would resume training for space shuttle Endeavour's two-week mission, which is targeted for liftoff from Cape Canaveral, Fla., on April 19. When asked if Giffords might be well enough to attend his launch, Kelly said: "Absolutely. I have every intention that she'll be there for the launch. I've already talked to her doctors about it." It will be Endeavour's final flight and the fourth spaceflight for Kelly.

Kelly said the congresswoman continues to improve in rehab in Houston. One doctor has described her recovery as "lightning speed." She's kept very busy with therapy, a key to his decision, he said. The 40-year-old Giffords was in intensive care for two weeks in Arizona, with Kelly at her bedside, before she was transferred to Houston for what is expected to be a lengthy rehabilitation. Kelly wanted her as close to him as possible, if he returned to work at Johnson Space Center. He lives in the Houston area with his two teenage daughters from a previous marriage, Claudia and Claire.

Giffords was meeting with constituents outside a Tucson supermarket when she was shot in the head. Six people were killed and 13 were injured in the rampage; a 22-year-old suspect is in custody.

Giffords' wound was devastating, and Kelly, 46, said he initially expected to step down as commander of Endeavour. In the meantime, NASA named a backup commander, Rick Sturckow, who joined the crew for training. Kelly said all along that he wanted his wife's input in the matter, if at all possible. Though doctors described her early progress as remarkable, they have said very little about her condition, including whether she's able to speak. She was shot in the left side of her brain and doctors have said she had weakness on her right side. In the first several days after the shooting, she gave a thumbs up and was able to stand with help. She massaged her husband's neck, picked out colors on an iPad and playfully took the ring off a nurse's finger. Friends and Kelly described her as able to understand them.

Her hospital, TIRR Memorial Hermann, last week said it would not provide any more information on her condition. In a Twitter update Wednesday, her husband said Giffords is making "Lots of progress!"

"I'm not going to second guess his decision for anything. I respect his decision, I'm sure it's the decision that Gabby would have wanted him to make and I'm sure he has the support of his family and friends there," said former astronaut Susan Still Kilrain, who gave up her astronaut career when she had the first of her four children.

Kelly - whose identical twin Scott currently is commander of the International Space Station - will lead a veteran, all-male, American-Italian crew to the space station. Scott Kelly will be back on Earth by then.

There's considerable training between now and liftoff, almost certainly with long hours and few days off for the crew. The six astronauts will go into quarantine a week before the launch, with limited access to family members. "I obviously weigh time that I can spend with her, with what I think is in the best interest of NASA and my crew. So that's a debate I had with myself," Kelly said.

Kelly's mission already was set to be one of the highest profile shuttle flights ever. It will be Endeavour's last voyage and the next-to-last for the entire 30-year shuttle program, and will feature the delivery of an elaborate physics experiment by a Nobel prize winner. Endeavour was originally scheduled to launch last July, but was bumped into 2011 because the experiment wasn't ready.

Susan Hileman, who was wounded in Tucson, trusts Kelly's decision. She was holding 9-year-old Christina Green's hand when the shooting erupted. The girl was killed. "I'm sure this decision was carefully made and thoughtfully made, and right for him and for them," said Hileman, who was shot three times. "He's kind and thoughtful and he loves his wife as much as my husband loves me, which is a lot, and we're both lucky women to have such strong men in our lives."

Rabbi Stephanie Aaron, who married Giffords and Kelly in 2007, said the couple has been communicating but she didn't elaborate. "I think that once he saw that Gabby was so strong and on the mend .... that he made the decision based on, I'm sure, what her wishes would be," Aaron said. *More information: NASA:*

<http://www.nasa.gov/shuttle>

<http://www.physorg.com/news/2011-02-brains-smarter.html>

### **Are brains shrinking to make us smarter?**

***Human brains have shrunk over the past 30,000 years, puzzling scientists who argue it is not a sign we are growing dumber but that evolution is making the key motor leaner and more efficient.***

The average size of modern humans - the Homo sapiens - has decreased about 10 percent during that period - from 1,500 to 1,359 cubic centimeters, the size of a tennis ball. Women's brains, which are smaller on average than those of men, have experienced an equivalent drop in size. These measurements were taken using skulls found in Europe, the Middle East and Asia.

"I'd called that a major downsizing in an evolutionary eye blink," John Hawks of the University of Michigan told Discover magazine. But other anthropologists note that brain shrinkage is not very surprising since the stronger and larger we are, the more gray matter we need to control this larger mass.

The Neanderthal, a cousin of the modern human who disappeared about 30 millennia ago for still unknown reasons, was far more massive and had a larger brain. The Cro-Magnons who left cave paintings of large animals in the monumental Lascaux cave over 17,000 years ago were the Homo sapiens with the biggest brain. They were also stronger than their modern descendants.

Psychology professor David Geary of the University of Missouri said these traits were necessary to survive in a hostile environment. He has studied the evolution of skull sizes 1.9 million to 10,000 years old as our ancestors and cousins lived in an increasingly complex social environment. Geary and his colleagues used population density as a measure of social complexity, with the hypothesis that the more humans are living closer together, the greater the exchanges between group, the division of labor and the rich and varied interactions between people. They found that brain size decreased as population density increased. "As complex societies emerged, the brain became smaller because people did not have to be as smart to stay alive," Geary told AFP.

But the downsizing does not mean modern humans are dumber than their ancestors - rather, they simply developed different, more sophisticated forms of intelligence, said Brian Hare, an assistant professor of anthropology at Duke University. He noted that the same phenomenon can be observed in domestic animals compared to their wild counterparts. So while huskies may have smaller brains than wolves, they are smarter and more sophisticated because they can understand human communicative gestures, behaving similarly to human children. "Even though the chimps have a larger brain (than the bonobo, the closest extant relative to humans), and even though a wolf has a much larger brain than dogs, dogs are far more sophisticated, intelligent and flexible, so intelligence is not very well linked to brain size," Hare explained.

He said humans have characteristics from both the bonobo and chimpanzee, which is more aggressive and domineering. "The chimpanzees are violent because they want power, they try to have control and power over others while bonobos are using violence to prevent one for dominating them," Hare continued. "Humans are both chimps and bobos in their nature and the question is how can we release more bonobo and less chimp.

"I hope bonobos win... it will be better for everyone," he added.

[http://www.eurekalert.org/pub\\_releases/2011-02/hu-cbm020411.php](http://www.eurekalert.org/pub_releases/2011-02/hu-cbm020411.php)

### Clay-armored bubbles may have formed first protocells

#### **Discovery of inorganic, semipermeable clay vesicles indicates minerals could have played a key role in the origins of life**

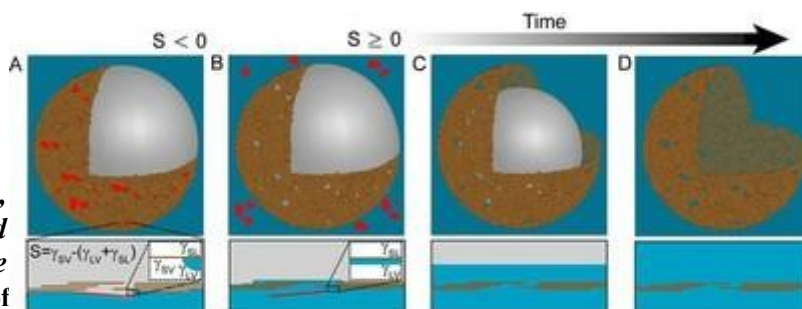
Cambridge, Mass. – A team of applied physicists at Harvard's School of Engineering and Applied Sciences (SEAS), Princeton, and Brandeis have demonstrated the formation of semipermeable vesicles from inorganic clay.

The research, published online this week in the journal *Soft Matter*, shows that clay vesicles provide an ideal container for the compartmentalization of complex organic molecules. The authors say the discovery opens the possibility that primitive cells might have formed inside inorganic clay microcompartments.

"A lot of work, dating back several decades, explores the role of air bubbles in concentrating molecules and nanoparticles to allow interesting chemistry to occur," says lead author Anand Bala Subramaniam, a doctoral candidate at SEAS. "We have now provided a complete physical mechanism for the transition from a two-phase clay-air bubble system, which precludes any aqueous-phase chemistry, to a single aqueous-phase clay vesicle system," Subramaniam says, "creating a semipermeable vesicle from materials that are readily available in the environment."

"Clay-armored bubbles" form naturally when platelike particles of montmorillonite collect on the outer surface of air bubbles under water. When the clay bubbles come into contact with simple organic liquids like ethanol and methanol, which have a lower surface tension than water, the liquid wets the overlapping plates.

*The authors' schematic of clay vesicle formation, showing a cut-away view of the clay shell and dissolving bubble at the top, and a view of the water-air interface at the bottom. Image courtesy of Anand Bala Subramaniam, Harvard School of*



Engineering and Applied Sciences.

As the inner surface of the clay shell becomes wet, the disturbed air bubble inside dissolves. The resulting clay vesicle is a strong, spherical shell that creates a physical boundary between the water inside and the water outside. The translucent, cell-like vesicles are robust enough to protect their contents in a dynamic, aquatic environment such as the ocean. Microscopic pores in the vesicle walls create a semipermeable membrane that allows chemical building blocks to enter the "cell," while preventing larger structures from leaving. Scientists have studied montmorillonite, an abundant clay, for hundreds of years, and the mineral is known to serve as a chemical catalyst, encouraging lipids to form membranes and single nucleotides to join into strands of RNA.

Because liposomes and RNA would have been essential precursors to primordial life, Subramaniam and his coauthors suggest that the pores in the clay vesicles could do double duty as both selective entry points and catalytic sites. "The conclusion here is that small fatty acid molecules go in and self-assemble into larger structures, and then they can't come out," says principal investigator Howard A. Stone, the Dixon Professor in Mechanical and Aerospace Engineering at Princeton, and a former Harvard faculty member. "If there is a benefit to being protected in a clay vesicle, this is a natural way to favor and select for molecules that can self-organize."

Future research will explore the physical interactions between the platelike clay particles, and between the liquids and the clay. The researchers are also interested to see whether these clay vesicles can, indeed, be found in the natural environment today. "Whether clay vesicles could have played a significant role in the origins of life is of course unknown," says Subramaniam, "but the fact that they are so robust, along with the well-known catalytic properties of clay, suggests that they may have had some part to play."

*Subramaniam and Stone's coauthors include Jiandi Wan, of Princeton University, and Arvind Gopinath, of Brandeis University.*

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