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## **Researchers warn of the 'myths' of global medical tourism**

*A team of British researchers, led by the University of York, is warning governments and healthcare decision makers across the globe to be wary of the myths and hype surrounding medical tourism.*

In an article, to be published in the journal Policy & Politics by Policy Press, the researchers challenge the idea that ever greater numbers of patients are prepared to travel across national borders to receive medical treatment. 'Medical tourism' is where people leave their own country to seek medical treatment abroad. They are typically treated as private patients and the costs are fully recouped. This is distinct from 'health tourism' where there is not always an intention to pay.

In the article, the authors, who include academics from the London School of Hygiene & Tropical Medicine, Royal Holloway University, and the University of Birmingham, looked beyond the NHS and the UK to address the wider international issues of medical tourism, examining how other countries are addressing this global phenomenon.

They describe 'three myths' of medical tourism: the rise and rise of medical tourism; enormous global market opportunities; and that national governments have a role to play in stimulating the medical tourism sector through high-tech investment. The researchers say these three widely-held assumptions cannot be backed up with hard evidence but are encouraged by interested parties such as healthcare providers, and brokers and facilitators who act as intermediaries between providers and patients.

Lead author Dr Neil Lunt, from the University of York's Department of Social Policy and Social Work, said: "In the past decade or so, the global health policy literature and consultancy reports have been awash with speculations about patient mobility, with an emphasis on how ever greater numbers of patients are travelling across national jurisdictions to receive medical treatments.

"Yet authoritative data on numbers and flows of medical tourists between nations and continents is tremendously difficult to identify. What data does exist is generally provided by stakeholders with a vested interest rather than by independent research institutions. What is clear is that there exists no credible authoritative data at the global level, which is why we are urging caution to governments and other decision-makers who see medical tourism as a lucrative source of additional revenue.

"Our message is: be wary of being dazzled by the lure of global health markets, and of chasing markets that do not exist." The paper was informed by a research project funded by the National Institute for Health Research Health Services and Delivery Research (NIHR HS&DR) Programme. It uses the findings from a two-year study into the impact of medical tourism on the UK's health system to make broader observations which the researchers believe apply to medical tourism globally.

The report authors argue that in terms of medical tourism, a level playing field does not necessarily exist and they challenge the view of open and global markets. Networks, history and relationships, they say, may explain a great deal about the success of particular destinations.

Dr Daniel Horsfall, from York's Department of Social Policy and Social Work, who carried out the statistical analysis for the study, said: "We found that historical flows between different countries and cultural relations account for a great deal of the trade. The destinations of medical tourists are typically based on geo-political factors, such as colonialism and existing trade patterns. For example, you find that medical tourists from the Middle East typically go to Germany and the UK due to existing ties, while Hungary attracts medical tourists from Western Europe owing to its proximity."

The team of researchers has already published an Organisation for Economic Co-operation and Development (OECD) report on their findings, while Dr Lunt has delivered their message of caution to the World Health Organisation and the Portuguese and Ukraine Governments. On 6 November, Dr Lunt will be a speaker at a professional networking event organised by the magazine Scientific American which will address trends in medical tourism.

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## **Why tumor cells go on dangerous tours**

*Tumors become highly malignant when they acquire the ability to colonize other tissues and form metastases. Researchers at Ludwig-Maximilians-Universitaet (LMU) in Munich have identified a factor that promotes metastasis of colon tumors – and presents a possible target for therapy.*

The protein c-MYC is referred to as a master regulator because it controls the activity of hundreds of genes, including many that drive cell growth and cell proliferation. Genetic changes that perturb its own regulation therefore have serious consequences for tissue homeostasis, and often result in cancer. Indeed, in most cancers, one finds mutations that hyperactivate the c-MYC gene. Furthermore, the c-MYC protein also plays a crucial

role in metastasis – the seeding of satellite tumors in other tissues by cells from the primary tumor – because it also stimulates the so-called epithelial-mesenchymal transition (EMT). In consequence, hyperactive c-MYC converts tumor cells that are proliferating non-invasively within the confines of an epithelial sheet into mobile cells with metastatic potential that leave the epithelium and can invade, and establish new tumors in distant tissues.

"Using colorectal cancer as a model, we have asked whether the protein ZNF281, which we have shown to interact with c-MYC in an earlier study, plays a role in the process of metastasis," says Professor Heiko Hermeking of the Institute of Pathology at the LMU, whose work focuses on the molecular bases of carcinogenesis. Since little was known about the mechanisms that control the ZNF281 gene itself, he and his research group took a closer look at its regulatory segment, or promoter. Their findings revealed that ZNF281 is at the hub of a complex functional network that indeed has a significant influence on tumor metastasis.

"The ZNF281 promoter sequence contains several binding sites for the SNAIL protein, which is in turn involved in implementing the EMT triggered by c-MYC, and we were able to show that the metastasis-promoting role of SNAIL depends on its ability to bind to the ZNF281 promoter," says Hermeking. In addition, the researchers demonstrated that the ZNF281 protein itself activates SNAIL, thus setting up a positive feedback loop that further increases its own expression. However, ZNF281 also directly activates other genes whose products drive the EMT, so that its role in establishing new tumors in distant tissues is not solely dependent on its interaction with SNAIL.

### **ZNF281 is essential for metastasis**

The amount of ZNF281 in cells is normally limited by the action of the microRNA miR-34a, a short RNA molecule that inhibits its synthesis by a mechanism known as RNA interference. Transcription of miRNA-34a gene is in turn inhibited by SNAIL. Thus, SNAIL also acts at this level to raise the concentration of ZNF281 in the cell. Earlier work by Hermeking's group had shown that transcription of miR-34a is induced by the tumor suppressor p53, and that this interaction is part of a protective mechanism that inhibits the EMT and thus prevents metastasis. SNAIL therefore promotes metastasis by stimulating the production of the ZNF281 protein via two distinct mechanisms. It activates transcription of the messenger RNA (mRNA) encoding ZNF281, and it represses expression of miRNA-34a, which would otherwise inhibit the synthesis of ZNF281 directed by the ZNF281 mRNA. This type of two-pronged regulatory mechanism is referred to as feed-forward regulation. The researchers confirmed the central role of ZNF281 in metastasis by demonstrating that in mice, colon cancer cells that lack the ZNF281 protein do not metastasize to the lung. "Inhibition of ZNF281 prevents metastasis, at least in mice. So it might be possible to inhibit the formation of new metastatic tumors or eliminate pre-existing ones using therapeutic agents directed against ZNF281," Hermeking concludes. "Furthermore, the presence of ZNF281 in primary tumors could be used as a prognostic marker that allows one to estimate the likelihood of metastatic tumors appearing after surgical removal of the primary tumor." Hermeking and his colleagues now hope to define the role of ZNF281, and therefore its potential as a target for anti-metastatic drugs, more precisely.

[http://www.eurekalert.org/pub\\_releases/2013-11/uoc--aak103113.php](http://www.eurekalert.org/pub_releases/2013-11/uoc--aak103113.php)

### **Astronomers answer key question: How common are habitable planets?**

*Based on Kepler data, 1 in 5 sun-like stars has Earth-size planet in habitable zone*

NASA's Kepler spacecraft, now crippled and its four-year mission at an end, nevertheless provided enough data to complete its mission objective: to determine how many of the 100 billion stars in our galaxy have potentially habitable planets. Based on a statistical analysis of all the Kepler observations, University of California, Berkeley, and University of Hawaii, Manoa, astronomers now estimate that one in five stars like the sun have planets about the size of Earth and a surface temperature conducive to life.

"What this means is, when you look up at the thousands of stars in the night sky, the nearest sun-like star with an Earth-size planet in its habitable zone is probably only 12 light years away and can be seen with the naked eye. That is amazing," said UC Berkeley graduate student Erik Petigura, who led the analysis of the Kepler data. "It's been nearly 20 years since the discovery of the first extrasolar planet around a normal star. Since then we have learned that most stars have planets of some size and that Earth-size planets are relatively common in close-in orbits that are too hot for life," said Andrew Howard, a former UC Berkeley post-doctoral fellow who is now on the faculty of the Institute for Astronomy at the University of Hawaii. "With this result we've come home, in a sense, by showing that planets like our Earth are relatively common throughout the Milky Way galaxy."

Petigura, Howard and Geoffrey Marcy, UC Berkeley professor of astronomy, will publish their analysis and findings online the week of Nov. 4 in the journal Proceedings of the National Academy of Sciences.

**Earth-size may not mean habitable**

"For NASA, this number – that every fifth star has a planet somewhat like Earth – is really important, because successor missions to Kepler will try to take an actual picture of a planet, and the size of the telescope they have to build depends on how close the nearest Earth-size planets are," Howard said. "An abundance of planets orbiting nearby stars simplifies such follow-up missions."

The team cautioned that Earth-size planets in Earth-size orbits are not necessarily hospitable to life, even if they orbit in the habitable zone of a star where the temperature is not too hot and not too cold.

"Some may have thick atmospheres, making it so hot at the surface that DNA-like molecules would not survive. Others may have rocky surfaces that could harbor liquid water suitable for living organisms," Marcy said. "We don't know what range of planet types and their environments are suitable for life."

Last week, however, Howard, Marcy and their colleagues provided hope that many such planets actually are rocky. They reported that one Earth-size planet discovered by Kepler – albeit, a planet with a likely temperature of 2,000 Kelvin, which is far too hot for life as we know it – is the same density as Earth and most likely composed of rock and iron, like Earth. "This gives us some confidence that when we look out into the habitable zone, the planets Erik is describing may be Earth-size, rocky planets," Howard said.

**Transiting planets**

NASA launched the Kepler space telescope in 2009 to look for planets that cross in front of, or transit, their stars, which causes a slight diminution – about one hundredth of one percent – in the star's brightness. From among the 150,000 stars photographed every 30 minutes for four years, NASA's Kepler team reported more than 3,000 planet candidates. Many of these are much larger than Earth – ranging from large planets with thick atmospheres, like Neptune, to gas giants like Jupiter – or in orbits so close to their stars that they are roasted. To sort them out, Petigura and his colleagues are using the Keck Telescopes in Hawaii to obtain spectra of as many stars as possible. This will help them determine each star's true brightness and calculate the diameter of each transiting planet, with an emphasis on Earth-diameter planets.

Independently, Petigura, Howard and Marcy focused on the 42,000 stars that are like the sun or slightly cooler and smaller, and found 603 candidate planets orbiting them. Only 10 of these were Earth-size, that is, one to two times the diameter of Earth and orbiting their star at a distance where they are heated to lukewarm temperatures suitable for life. The team's definition of habitable is that a planet receives between four times and one-quarter the amount of light that Earth receives from the sun.

**A census of extrasolar planets**

What distinguishes the team's analysis from previous analyses of Kepler data is that they subjected Petigura's planet-finding algorithms to a battery of tests in order to measure how many habitable zone, Earth-size planets they missed. Petigura actually introduced fake planets into the Kepler data in order to determine which ones his software could detect and which it couldn't. "What we're doing is taking a census of extrasolar planets, but we can't knock on every door. Only after injecting these fake planets and measuring how many we actually found, could we really pin down the number of real planets that we missed," Petigura said.

Accounting for missed planets, as well as the fact that only a small fraction of planets are oriented so that they cross in front of their host star as seen from Earth, allowed them to estimate that 22 percent of all sun-like stars in the galaxy have Earth-size planets in their habitable zones.

"The primary goal of the Kepler mission was to answer the question, When you look up in the night sky, what fraction of the stars that you see have Earth-size planets at lukewarm temperatures so that water would not be frozen into ice or vaporized into steam, but remain a liquid, because liquid water is now understood to be the prerequisite for life," Marcy said. "Until now, no one knew exactly how common potentially habitable planets were around Sun-like stars in the galaxy."

All of the potentially habitable planets found in their survey are around K stars, which are cooler and slightly smaller than the sun, Petigura said. But the team's analysis shows that the result for K stars can be extrapolated to G stars like the sun. Had Kepler survived for an extended mission, it would have obtained enough data to directly detect a handful of Earth-size planets in the habitable zones of G-type stars.

"If the stars in the Kepler field are representative of stars in the solar neighborhood, ... then the nearest (Earth-size) planet is expected to orbit a star that is less than 12 light-years from Earth and can be seen by the unaided eye," the researchers wrote in their paper. "Future instrumentation to image and take spectra of these Earths need only observe a few dozen nearby stars to detect a sample of Earth-size planets residing in the habitable zones of their host stars."

In January, the team reported a similar analysis of Kepler data for scorched planets that orbit close to their stars. The new, more complete analysis shows that "nature makes about as many planets in hospitable orbits as in close-in orbits," Howard said.

The research was funded by UC Berkeley and the National Science Foundation, with the assistance of the Keck Observatories and NASA.

<http://phys.org/news/2013-11-crater-abode-life.html>

## A crater as an abode for life

*A new study shows how the heat generated from an asteroid impact could lead to a crater becoming a refuge for life, or even a potential birthplace for life's origin.*

An asteroid or comet smashing into the surface of a planet can spell doom for living creatures, but if the impact isn't large enough to completely decimate a planet's inhabitants, then the impact crater can ultimately provide a habitat for life. This is the finding of a new study reported at the European Planetary Science Congress in September by Iain Gilmour of the Open University in the UK.

If an ice or water-rich target is the victim of an impact, the combination of heat and groundwater will create what is known as a hydrothermal system. In addition, many complex organic compounds, which could be precursor molecules for life, are created at high temperatures such as those in a collision. This combination could create the ingredients needed for life as we know it, making impact-induced habitats a potential candidate for the birthplace of life on Earth.



*Pingaluit crater in Canada is a geologically-young impact crater with a lake. Credit: NASA*

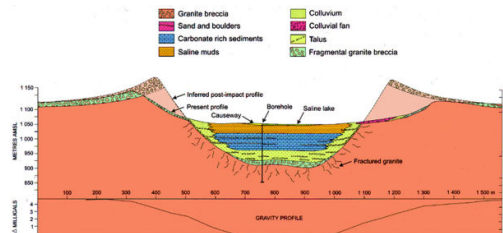
For a habitat within a crater to remain "home sweet home," there must be a constant supply of water and nutrients. The lifetime of the hydrothermal system is also crucial, as the heat from the impact will eventually fade away into its surroundings.

Measuring the cooling time of an ancient crater can shed light on the importance of such an abode in the origins of life, and also probe how a crater can provide a habitable niche for microbial life on other planets.

The Boltysh crater in the Ukraine makes the perfect target for such an investigation, so Gilmour and his colleagues investigated the heating timescale of the crater.

The 24 kilometer diameter crater was created around 65 million years ago, and predates the Chicxulub crater - the smoking gun from the asteroid impact that wiped out the dinosaurs - by a few thousand years. Shortly after the impact that formed the Boltysh crater, a lake formed within it, laying down layers of sediments over time.

In 2008, Gilmour and his team drilled a 596 meter borehole to sample these sediments, and found that the post-impact sedimentary record at this crater is well preserved, enabling the scientists to reconstruct the thermal history of the crater.



*A cross section of the Tswaing crater in South Africa shows how the layers of sediments that have been deposited over time can be sampled by drilling a borehole. Credit: Brandt, D., (1994), Brandt & Reimold (1999), Partridge & Reimold (1990)*

### Taking the temperature of the crater

Different techniques can be used to persuade the sediments to reveal their past. One of the methods used by the scientists utilized molecules known as isomers, which have the same chemical formula but different structures. Certain types of isomers are sensitive to heat, and the level of isomers will deplete at a certain rate when they are in the vicinity of a heat source. At the bottom of the Boltysh crater core, which samples the layers of sediments laid down directly above the impact site, the levels of two different isomers drop significantly. The thermal degradation of the isomers can be measured experimentally, so it is known that the temperature of the lake was between 75 and 250 degrees Celsius for a time after the impact.

As the isomers are only depleted in a few meters of the core above the impact site, it is possible to place a limit on the heating duration. However, the isomers cannot reveal the source of the heat, which is why another experimental technique was used to characterize the post-impact heating.

This technique involved measuring the composition of certain isotopes within carbonates in the sediments. Isotopes of the same element have the same number of protons and electrons, but different numbers of neutrons. While such isotopes can undergo the same chemical reactions, the rate of reactions will be quicker for some isotopes. For instance, evaporation will deplete heavier isotopes while enriching lighter ones, leaving different levels of the isotopes.

Evaporation of a lake is strongly dependent on the amount of time that it takes for water to flow into and out of the lake, and this "flushing time" is recorded by the isotopes in the lake sediments. The flushing time will be altered by groundwater, heated from the impact, bubbling up through fissures into the lake. The isotope



compositions of the Boltysch crater can thus be used to estimate the heating time by seeing how long the water in the lake interacted with the hydrothermal groundwater.

The sediments also contain minute traces of vegetation, and changes in the vegetation over time can be linked to changes in the environment. The flora at the bottom of the core reveal that vegetation had been recovering for a few thousand years after the Boltysch impact, until the Cretaceous–Paleogene impact decimated the vegetation, along with the dinosaurs. The sediments also record changes in carbon which coincide with a period of warming during the first few hundred thousand years of the early Paleogene. These events act as bookends, making it easier to date the sediments and thus the heating timescale of the lake.

The results show that the hydrothermal system at Boltysch persisted for somewhere between 30,000 and 40,000 years, and it seems that the presence of the lake significantly extended the heating time.

Haughton crater, which is of a similar size to Boltysch, should have a comparable timescale for its hydrothermal system. However, Haughton crater did not fill up with a lake until millions of years after the impact, long after the hydrothermal system had cooled, and subsequently its heating timescale was only 5,000 years.

The formation of a lake and its longevity could be key factors in a crater being a home for life.

### **Craters as habitats in the Solar System**

"The cooling timescale, at 30,000 to 40,000 years, is not that long when one considers that after it's cold then it may not remain a viable habitat," said Gilmour. "The question then becomes one of cratering flux on early planets and whether that flux is enough to create interlinked habitats, but not so great as to potentially wipe out life."

Such a heating timescale suggests that in moderately sized craters, the heating may not have been significant enough to destroy all existing life, so microbial life might have survived.

Many craters on Mars are of a similar size, so there could still be a record of organic matter if the sediments that carry this information are preserved. This is why NASA's Curiosity rover is currently rummaging around in the Gale crater on Mars searching for any signs of a past habitat.

A crater etched into the landscape of a planet is not only the fingerprint of the rogue Solar System body that caused the collision, it also provides clues to the impact on life after such an event. Knowledge of the heating duration of the Boltysch crater therefore is a step forward in understanding how collisions influence life, both on Earth and on other planets.

Source: *AstroBio.net*

<http://www.medscape.com/viewarticle/813762?src=rss>

### **Analgesic Overuse May Fuel Persistent Headache After Concussion**

*Overuse of analgesics after concussion may exacerbate concussion-related headaches or make them chronic, a new study suggests.*

Megan Brooks

AUSTIN, Texas - The researchers advise minimizing analgesics or discontinuing them when headaches continue several weeks after the concussion. Geoffrey L. Heyer, MD, and Syed A. Idris, MD, from Nationwide Children's Hospital in Columbus, Ohio, reported their findings here at the Child Neurology Society (CNS) 2013 Annual Meeting.

Nationwide Children's Hospital is developing a complex concussion clinic through the pediatric neurology division, Dr. Heyer told Medscape Medical News. "Over the past 3 years, sports medicine doctors and pediatricians/primary care doctors have been sending us their concussion patients who have persistent postconcussion symptoms, often lasting several months," he said. "We began noticing that a lot of these adolescents and young adults had been instructed to take analgesics during their acute concussion management, but the medicines were never decreased or stopped as the headaches became chronic," Dr. Heyer explained. By the time patients reached the clinic, many had been taking over-the-counter analgesics 2 to 3 times daily for many months for their daily or near-daily headaches, Dr. Heyer said. "As frequent and prolonged use of headache medicines (including simple analgesics) can cause a medication overuse headache, we decided to look back at patient outcomes once the analgesics were stopped," he noted.

### **Headaches Ease When Medication Stopped**

In reviewing 104 adolescent patients with concussion, the researchers found that 77 had chronic post-traumatic headache lasting between 3 and 12 months. Fifty-four of these patients (70.1%) met criteria for probable medication-overuse headache. Patients with medication overuse were more likely to have daily headaches ( $P = .006$ ), to be female ( $P = .02$ ), to have nausea ( $P < .001$ ), or to have throbbing associated with their headaches ( $P = .001$ ).

More than two thirds of the patients with medication overuse (37 of 54 [68.5%]) saw their headaches subside or improve to preconcussion patterns within 2 months of stopping analgesics. Seven patients (13%) had no change

in headache status or worsening of headaches after going off analgesics. Ten (18.5%) patients did not discontinue analgesics or were lost to follow-up.

"When daily headaches following concussion (post-traumatic headaches) continue for several weeks, clinicians should consider stopping analgesics or restricting their use to no more than 2 days weekly as medication-overuse headache can develop," Dr. Heyer said.

### **Tough to Draw Firm Conclusions**

"We need to remember that this is a poster with limited information," cautioned Rosemarie Scolaro Moser, PhD, board-certified neuropsychologist and director of the Sports Concussion Center of New Jersey, Lawrenceville.

"This research is a beginning, an initial look at an important issue, but not conclusive, as more controlled research needs to be conducted. The study documents correlations, not causation," added Dr. Moser, who wasn't involved in the study.

The fact that 68.5% of patients with medication-overuse headache had resolution of headaches or return to their preconcussion headache after discontinuing the medication "could also be explained by spontaneous healing; concussions do resolve and get better on their own, so I am not sure if taking the patients off the analgesics was what made them get better over a 2-month period," Dr. Moser told Medscape Medical News.

She cautioned that it's hard to make clinical conclusions based on this preliminary study. "I would recommend that parents and adolescents work with physicians and headache specialists who understand concussion and are careful about monitoring the use of any medications during the recovery period," Dr. Moser said.

"In addition, aside from medication, for chronic headaches, working with a neuropsychologist, psychotherapist, and biofeedback specialist may offer additional interventions to help alleviate the symptoms of headache," she added. *The authors and Dr. Moser have disclosed no relevant financial relationships.*

<http://www.sciencedaily.com/releases/2013/11/131104101049.htm>

### **Mutations Linked to Breast Cancer Treatment Resistance**

*Researchers at the University of Michigan Comprehensive Cancer Center have identified a type of mutation that develops after breast cancer patients take anti-estrogen therapies.*

The mutations explain one reason why patients often become resistant to this therapy. The study appears online in Nature Genetics.

The discovery stems from a program at the U-M Comprehensive Cancer Center called Mi-ONCOSEQ in which patients with advanced cancer have their DNA and RNA sequenced to identify all types of genetic mutations that could play a role in the cancer. Researchers use the findings to help direct therapies they think will work best. But they also use the data to find new genetic links. The detailed analysis means that researchers can identify anomalies among a small number of patients.

In this case, they looked at 11 patients with metastatic breast cancer that was classified as estrogen receptor positive, meaning the cancer is influenced by the hormone estrogen. This is the most common type of breast cancer. The analysis found that six patients had mutations in the estrogen receptor. All of them had been treated with an aromatase inhibitor, a type of drug that blocks estrogen production.

What's more, the researchers found that the mutations were not present before the patients started their treatment, which means it was the therapy itself that caused the mutations to develop or be selected.

"This is the tumor's way of evading hormonal therapy. These mutations activate the estrogen receptor when there is no estrogen -- as is the case when a patient takes an aromatase inhibitor. It's essentially an on-switch for the estrogen receptor," says lead study author, Dan Robinson, Ph.D., research assistant professor of pathology at the U-M Medical School.

This on-switch essentially circumvents the effects of the aromatase inhibitor, preventing estrogen receptor signaling from being shut down. That's when patients become resistant to the therapy, which leaves them with few other treatment options. Some 40,000 people will die from breast cancer this year in the United States, with the majority having estrogen receptor positive tumors.

"We've been trying for a long time to understand why people become resistant to anti-hormone therapy. This finding sheds an entirely new light onto the problem. Now, we can look at how these estrogen receptors function and begin to develop drugs to shut down or attack this mutation," says study co-author Anne F. Schott, M.D., associate professor of internal medicine at the U-M Medical School.

The researchers also suggest that blood tests could be used to monitor patients and detect these mutations to potentially shift treatment before resistance develops. It's not yet known how frequently these mutations in the estrogen receptor occur. Currently, no treatment exists to target the mutations.

"Precision medicine approaches will allow us to understand how targeted therapies are working, but another important challenge is to understand the mechanisms by which tumors become resistant to these treatments so

that we can prevent the resistance or develop strategies to overcome it," says senior study author Arul Chinnaiyan, M.D., Ph.D., director of the Michigan Center for Translational Pathology and S.P. Hicks Professor of Pathology at the U-M Medical School.

*Dan R Robinson, Yi-Mi Wu, Pankaj Vats, Fengyun Su, Robert J Lonigro, Xuhong Cao, Shanker Kalyana-Sundaram, Rui Wang, Yu Ning, Lynda Hodges, Amy Gursky, Javed Siddiqui, Scott A Tomlins, Sameek Roychowdhury, Kenneth J Pienta, Scott Y Kim, J Scott Roberts, James M Rae, Catherine H Van Poznak, Daniel F Hayes, Rashmi Chugh, Lakshmi P Kunju, Moshe Talpaz, Anne F Schott, Arul M Chinnaiyan. Activating ESRI mutations in hormone-resistant metastatic breast cancer. Nature Genetics, 2013; DOI: 10.1038/ng.2823*

<http://bit.ly/1cHGeyr>

## **Single atom catalyst suggests we don't understand catalysis that well**

**75% of reactions are due to 25% percent of atoms; the rest are lazy slackers.**

by Chris Lee - Nov 5 2013, 2:33am TST

If you ever wanted to name a single technology that transformed society while remaining nearly invisible, catalysts would be an excellent answer. Transforming one stable compound (say, nitrogen gas) into another stable compound (nitrogen-based fertilizer, for instance) requires an enormous amount of energy unless a catalyst is used. Then it suddenly becomes worthwhile. Indeed, that one reaction series - nitrogen gas to ammonia to fertilizer - is responsible for feeding the majority of people on the planet today.

The difficulty is that we don't really have a great understanding of how most catalysts work. And a recent paper adds considerably to that confusion by showing that single atoms can act as very efficient catalysts.

### **Why are catalysts necessary?**

When we make new compounds, whether they're plastics, gasoline, fertilizers, or pretty much any modern material, we require a catalyst at some point. The reason for this is simple. We take raw materials from the world around us. These materials are stable. If they weren't, they would have reacted long ago to form a different material that was stable. Stable materials like to stay just as they are.

The materials that we want to form are also stable. (Yes, even most explosives are relatively stable - the last thing you want is an explosive that will go off in your face because you dropped it.) The goal of most industrial chemistry is to transform a set of stable materials into a different set of stable materials. In order to do that, you need to add a lot of energy, much more than we are able to produce. If that was the end of the story, the latter part of the industrial revolution would have died in its infancy because its products would have been far too expensive. The trick of a catalyst is to reduce the amount of energy required at critical steps in the process. This is what makes most modern materials affordable.

### **How do catalysts work?**

No one is too sure how most catalysts work (there are some proteins that are pretty well understood). One thing is sure: all reactions take place at the surface of a catalyst. Increasing the available surface area of a catalytic material is one sure way to increase the efficiency of a catalyst, but we also know that not every surface atom in a catalyst material behaves as a catalyst. Imagine that you have a crystal of palladium atoms, roughly cut into a sphere. To make a sphere, you have a lot of edges and corners to crystalline planes. The atoms at the edges and corners are the ones that do the catalysis.

The hypothesis is that when something like a nitrogen molecule attaches to the corners and edges of a catalyst, it gets a bit distorted, making it a little easier to break the bonds between nitrogen atoms. In addition, the catalyst should be able to donate or accept electrons to aid the bond breaking process, so not just any material with crystalline edges can do the job. But frankly, this is all a little difficult to observe and confirm.

If this general picture were the whole story, the following experiment should not have produced the result that it did. Researchers from China and the US chose to study the production of hydrogen and carbon dioxide from water and carbon monoxide, a starting point for fuel production. One catalyst for this process is iridium, which is very expensive. In the ideal case, you want every iridium atom to play the role of the catalyst and use the smallest amount possible.

To achieve this, the researchers doped iron oxide with iridium at such low concentrations that most of the iridium atoms were alone in the iron oxide matrix. They used a bunch of very high-resolution imaging techniques to determine that at the lowest dopant concentrations (0.01 percent), the iridium atoms were almost always separated from each other by several iron oxide molecules. At higher concentrations, the iridium atoms started to clump together. These different samples provide a varying ratio between single iridium atoms and groups of iridium atoms.

By comparing the reaction rates between these different samples, the researchers were able to figure out how effective the single iridium atoms were. It turns out that even at the highest iridium concentrations (2.4 percent), single iridium atoms were responsible for 75 percent of the observed reaction products.

A catalytic reaction is a very complicated beast because it must proceed in steps that often involve molecules moving along the surface from one site to another. That movement is usually very slow, so the per-active-catalyst-site reaction rates are on the order of a single reaction per second. In this case, though, the single iridium atoms manage just over two reactions per second.

As far as I'm concerned, a more important fact is that at these concentrations, very few of the iridium atoms end up at corners or edges, so these structural features can only play a minor role. Indeed, for single atoms, it's very difficult to imagine how structure could play a role. Of course, flat surfaces without any edges will also catalyze reactions, but they are very slow and very ineffective. In this work, though, iridium atoms that were essentially part of a flat surface were both very effective and very fast, which means that I now have even less of a clue how this reaction proceeds.

Well, that's not entirely true. The iridium is not the same as the iron it replaces, so the crystal structure is a bit distorted at those points. Structure could still play a role, but these sorts of defects usually have to be at edges or corners to be as effective. In any case, my confusion is a good thing. By highlighting the shortcomings of a classic explanation for catalytic activity, new ideas will be generated.

*Journal of the American Chemical Society, 2013, DOI: 10.1021/ja408574m*

<http://www.livescience.com/40923-patagonia-bugs-survived-killer-impact.html>

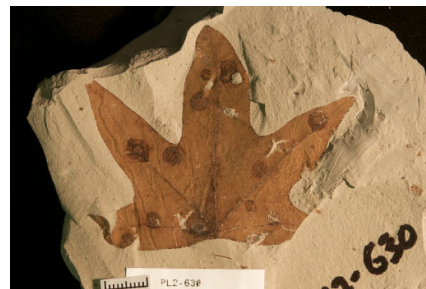
## Bugs in Patagonia Survived Dinosaur-Killing Impact

*There may be some truth to the old joke about only insects surviving an apocalypse.*

By Becky Oskin, Staff Writer | November 04, 2013 01:14pm ET

Down in Patagonia, thousands of miles from the site of the deadly asteroid impact in present-day Mexico that killed off the dinosaurs, most bugs easily survived one of Earth's worst mass extinctions 65 million years ago. The discovery adds to a growing body of evidence that the Cretaceous mass extinction had varied effects on species in different spots around the world.

Evidence from fossilized leaves suggests that, compared with insects in North America, a greater diversity of insects in South America chewed, sucked and otherwise fed off plants after the Cretaceous extinction, researchers reported Oct. 28 at the Geological Society of America's annual meeting in Denver.



***Leaf damage, such as chewing and galls, helps scientists track how insects weathered a Cretaceous asteroid impact that killed off the dinosaurs. Credit: Michael Donovan***

"There were devastating effects everywhere ... the dinosaurs did go extinct on every continent, obviously," said Michael Donovan, a graduate student at Pennsylvania State University. "Our results suggest the Southern extinction was different than what was seen in the North. It supports the emerging hypothesis of an early Paleocene refugium."

On both continents, insects from just before and after the Cretaceous-Paleocene extinction are rarely preserved as fossils, Donovan said. But there are thousands of leaf fossils and damage from insects, each of which ate in a unique way, which serve as a substitute for tracking species.

To track the extinction's effects on South American insects, Donovan has pored over about 3,000 leaf fossils from the Lefipán and Salamanca Formations in Argentina. The Salamanca rocks were deposited at about 50 degrees South latitude, during the Paleocene epoch.

The evidence suggests that before the impact, there was more diversity among bugs such as leaf miners, beetles, moths and flies in South America than in North America. After the mass extinction, both continents saw a decrease in diversity among bug species, but the drop was less severe in Patagonia, Donovan said.

The overall decrease in leaf damage types varied from 9 to 25 percent in Patagonia to 35 to 45 percent in fossils from the Western Interior Seaway, the great inland sea that once flooded western North America.

Among highly specialized insects, which chow down on only one or two kinds of plants, the die-offs were more severe closer to the impact site. There was only a 21 to 34 percent drop in leaf damage in Patagonia versus a 55 to 75 percent decrease in North America, Donovan said.

Pollen studies show a severe die-off in North American plants immediately after the impact. But pollen records confirm that the Patagonia insects' food source bounced back quickly after the asteroid hit Earth, according to a study published Dec. 17, 2012, in the journal PLOS ONE. Ocean plankton in the Southern Hemisphere also survived. "The insects were highly affected by what the asteroid did to their food," said Peter Wilf, a paleobotanist at Penn State and a co-author on both studies.

"The end Cretaceous extinction really does seem to be different than the story in North America," Wilf said.

"There seems to be much less of an extinction, and the recovery seems to be much faster."



<http://www.livescience.com/40925-king-tuts-death-spontaneous-combustion.html>

## Crashed and Burned: How King Tut Died

*Though the famed Egyptian pharaoh King Tutankhamun died more than 3,300 years ago, the mystery surrounding his death and mummification continues to haunt scientists.*

By Marc Lallanilla, Assistant Editor | November 04, 2013 01:31pm ET

Now, British researchers believe they've found evidence explaining how the boy king died and, in the process, made a shocking discovery: After King Tut was sealed in his tomb in 1323 B.C., his mummified body caught fire and burned.

Since Egyptologists Lord Carnarvon and Howard Carter uncovered King Tut's tomb in 1922, their discovery has been shrouded in mystery and fear. A "curse of the mummy's tomb" entered the popular imagination after several members of the archaeological team died untimely deaths.

Archaeologist Chris Naunton, director of the Egypt Exploration Society, recently came across comments in Carter's original notes stating that King Tut's body appeared to have been burned, the Independent reports. Naunton then contacted Egyptologist Robert Connolly of Liverpool University, who had small samples of Tutankhamun's bones and flesh in his office.

When the team examined the pharaoh's remains under an electron microscope, they found that the pharaoh's flesh did, indeed, burn after he was laid to rest inside a sealed tomb - an extremely odd event, given the meticulous attention usually afforded the mummification of a king.

These and other revelations are detailed in a new British documentary, "Tutankhamun: The Mystery of the Burnt Mummy," featuring Naunton's investigative work (which has not yet been published in a peer-reviewed journal). But how would the fire in Tut's sealed tomb have occurred?

### A hasty burial

Experts suspect the oils used in the embalming process soaked the linen that formed the king's burial shroud. In the presence of oxygen, these flammable oils started a chain reaction that ignited and "cooked" Tutankhamun's body at temperatures exceeding 390 degrees Fahrenheit (200 degrees Celsius).

For years, evidence has suggested the pharaoh was buried in haste - spots on the walls of Tut's tomb caused by microbial activity, for example, led researchers to believe that the paint on the walls hadn't even dried before the tomb was sealed. The additional evidence of an accidental burning lends credence to the idea that Tut's entire burial was basically a rush job.

"The charring and possibility that a botched mummification led to the body spontaneously combusting shortly after burial was entirely unexpected - something of a revelation," said Naunton, as quoted in the Independent.

### Is spontaneous combustion real?

Spontaneous human combustion, once considered an impossibility, has received renewed interest from scientists worldwide. British biologist and author Brian Ford believes that flammable acetone produced by a body could - in the presence of a spark from static electricity or some other ignition source - cause a human body to catch fire and burn.

And by analyzing the injuries sustained by car-crash victims, forensic scientists have now shed light on the events surrounding the death of the boy king, who is believed to have been just 17 years old when he died.

Investigators were able to determine that the young pharaoh was on his knees when a horrific chariot accident smashed his rib cage, shattered his pelvis and crushed many of his internal organs, including his heart, according to the Guardian. This may explain why his heart was never found in his mummified body.

<http://nyti.ms/1cIv4cB>

## Vaccine Approved for Brain Fever

*The World Health Organization has approved a new vaccine for a strain of encephalitis that kills thousands of children and leaves many survivors with permanent brain damage.*

By DONALD G. McNEIL Jr.

The move allows United Nations agencies and other donors to buy it. The disease, called Japanese encephalitis or brain fever, is caused by a mosquito-transmitted virus that can live in pigs, birds and humans. Less than 1 percent of those infected get seriously ill, but it kills up to 15,000 children a year and disables many more. Up to four billion people, from southern Russia to the Pacific islands, are at risk; it is more prevalent near rice paddies. There is no cure.

The low-cost vaccine, approved last month, is the first authorized by the agency for children and the first Chinese-made vaccine it has approved. It is made by China National Biotec Group and was tested by PATH, a nonprofit group in Seattle with funding from the Bill and Melinda Gates Foundation.

Dr. Margaret Chan, W.H.O.'s director-general, said she hoped that approval would encourage other vaccine makers from China and elsewhere to enter the field.

China had given the vaccine domestically to 200 million children over many years but had never sought W.H.O. approval. India, which previously bought 88 million doses from China, launched the first locally produced version last month.

A Novartis vaccine for Japanese encephalitis, Ixiaro, is approved by the Food and Drug Administration. But travel clinics charge \$200 or more for it. Two weeks after the W.H.O. approved the Chinese vaccine, the F.D.A. granted Ixiaro's maker seven years of exclusivity.

<http://www.bbc.co.uk/news/health-24805626>

### **Prostate cancer aggression test 'may avoid needless ops'**

*A prostate cancer test, which predicts how aggressive a tumour is, could spare men unnecessary operations, researchers suggest.*

**By James Gallagher Health and science reporter, BBC News**

Early data, presented at the National Cancer Research Institute conference, suggests a genetic test can tell apart aggressive and slow-growing tumours. A big challenge in treating the cancer is knowing whether surgery to remove the gland is needed. Cancer charities said a successful test would be a "game-changer".

Prostate cancer is the most common male cancer in the UK. There are more than 40,000 new cases diagnosed and 10,000 deaths each year.

#### **Tough choice**

The decision to remove the prostate is based on an examination of a tumour sample under the microscope. However, the procedure has significant side-effects such as infertility, difficulty maintaining and keeping an erection and uncontrolled urinating.

One of the researchers, Prof Dan Berney, from Queen Mary University of London, told the BBC: "We need a better test as we are over-treating many men; most will die with, not of, prostate cancer. "We need to discriminate between the aggressive forms and those that will grumble along and just need monitoring."

The commercial test, developed by Myriad Genetics but independently assessed by Queen Mary University of London, looks at the activity level of genes inside a sample of the tumour.

If 31 genes involved in controlling how cells divide are highly active, it indicates the cancer is aggressive.

Prof Berney said such information could "substantially change" decisions made by doctors and patients but the costs were "huge" and it was certainly not going to be offered on the NHS in the next few years.

"We need to validate it and we're not there yet, but it is the strongest test we've had so far," he added.

#### **'Intriguing'**

Dr Iain Frame, director of research at Prostate Cancer UK, said: "Developing an effective test to distinguish aggressive from non-aggressive prostate cancer could be a game-changer for those affected by the condition.

"We urgently need to reach a point where we can focus resources on saving more of the 10,000 men who lose their lives to this disease every year, whilst sparing the many others who needn't have concerns.

"The results of this study are certainly intriguing, and take us a step closer to the diagnostic process for prostate cancer that men deserve. We will watch with great interest developments in this area."

Dr Harpal Kumar, the chief executive of Cancer Research UK, said: "Being able to tell apart aggressive and slow-growing tumours would help us take a major step forward in prostate cancer treatment. "Understanding more about the nature of a patient's tumour could spare thousands of men from unnecessary treatment and the resulting side-effects, whilst also meaning that those who do need treatment receive it rapidly."

[http://www.eurekalert.org/pub\\_releases/2013-11/cu-cmh110513.php](http://www.eurekalert.org/pub_releases/2013-11/cu-cmh110513.php)

### **Clay may have been birthplace of life, new study suggests**

*Clay might have been the birthplace of life on Earth, or at least of life's complex biochemicals*

ITHACA, N.Y. – Clay, a seemingly infertile blend of minerals, might have been the birthplace of life on Earth. Or at least of the complex biochemicals that make life possible, Cornell University biological engineers report in the Nov. 7 online issue of the journal *Scientific Reports*, published by Nature Publishing.

"We propose that in early geological history clay hydrogel provided a confinement function for biomolecules and biochemical reactions," said Dan Luo, professor of biological and environmental engineering and a member of the Kavli Institute at Cornell for Nanoscale Science. **Study:** <https://cornell.box.com/clay>

In simulated ancient seawater, clay forms a hydrogel – a mass of microscopic spaces capable of soaking up liquids like a sponge. Over billions of years, chemicals confined in those spaces could have carried out the complex reactions that formed proteins, DNA and eventually all the machinery that makes a living cell work. Clay hydrogels could have confined and protected those chemical processes until the membrane that surrounds living cells developed.

To further test the idea, the Luo group has demonstrated protein synthesis in a clay hydrogel. The researchers previously used synthetic hydrogels as a "cell-free" medium for protein production. Fill the spongy material with DNA, amino acids, the right enzymes and a few bits of cellular machinery and you can make the proteins for which the DNA encodes, just as you might in a vat of cells.

To make the process useful for producing large quantities of proteins, as in drug manufacturing, you need a lot of hydrogel, so the researchers set out to find a cheaper way to make it. Postdoctoral researcher Dayong Yang noticed that clay formed a hydrogel. Why consider clay? "It's dirt cheap," said Luo. Better yet, it turned out unexpectedly that using clay enhanced protein production.

But then it occurred to the researchers that what they had discovered might answer a long-standing question about how biomolecules evolved. Experiments by the late Carl Sagan of Cornell and others have shown that amino acids and other biomolecules could have been formed in primordial oceans, drawing energy from lightning or volcanic vents. But in the vast ocean, how could these molecules come together often enough to assemble into more complex structures, and what protected them from the harsh environment?

Scientists previously suggested that tiny balloons of fat or polymers might have served as precursors of cell membranes. Clay is a promising possibility because biomolecules tend to attach to its surface, and theorists have shown that cytoplasm – the interior environment of a cell – behaves much like a hydrogel. And, Luo said, a clay hydrogel better protects its contents from damaging enzymes (called "nucleases") that might dismantle DNA and other biomolecules.

As further evidence, geological history shows that clay first appeared – as silicates leached from rocks – just at the time biomolecules began to form into protocells – cell-like structures, but incomplete – and eventually membrane-enclosed cells. The geological events matched nicely with biological events.

How these biological machines evolved remains to be explained, Luo said. For now his research group is working to understand why a clay hydrogel works so well, with an eye to practical applications in cell-free protein production.

*Luo collaborated with professor Max Lu of the Australian Institute for Bioengineering and Nanotechnology at the University of Queensland in Australia. The work was performed at the Cornell Center for Materials Research Shared Facilities, supported by the National Science Foundation.*

[http://www.eurekalert.org/pub\\_releases/2013-11/tes-eru110513.php](http://www.eurekalert.org/pub_releases/2013-11/tes-eru110513.php)

## **Experts recommend universal diabetes testing for pregnant women at first prenatal visit**

### ***Endocrine Society publishes Clinical Practice Guideline on diabetes and pregnancy***

Chevy Chase, MD - The Endocrine Society today issued a Clinical Practice Guideline (CPG) to help health care professionals provide the best care to pregnant women who have diabetes.

The CPG, entitled "Diabetes and Pregnancy: An Endocrine Society Clinical Practice Guideline" appeared in the November 2013 issue of the Journal of Clinical Endocrinology and Metabolism (JCEM), a publication of The Endocrine Society.

Experts acknowledge that cases of diabetes in pregnant women are being missed by traditional screening methods, said Ian Blumer, MD, of the Charles H. Best Diabetes Centre in Whitby, Ontario, Canada, and chair of the task force that authored the guideline. The Endocrine Society CPG recommends that all pregnant women who have not been previously diagnosed with diabetes be tested for the condition at their first prenatal visit.

The test should be done before 13 weeks' gestation or as soon as possible thereafter.

"Many women have type 2 diabetes but may not know it," Blumer said. "Because untreated diabetes can harm both the pregnant woman and the fetus, it is important that testing for diabetes be done early on in pregnancy so that if diabetes is found appropriate steps can be immediately undertaken to keep both the woman and her fetus healthy."

As many as one in five women may develop gestational diabetes – a form of diabetes that has its onset during pregnancy. Traditional testing strategies only identify about a quarter of these cases. This means that many women go undiagnosed and are at increased risk of having an overly large baby, which can complicate delivery.

"To address this problem, the CPG advocates for using lower blood glucose levels to diagnose gestational diabetes," Blumer said. "Using these lower levels will allow for the detection of gestational diabetes in many women when it would otherwise go undetected using the older diagnostic thresholds. Once the diagnosis is made, treatment can be given to help the fetus grow normally."

"Thanks to important new studies of the interplay between diabetes and pregnancy, diabetes specialists and obstetricians have identified best practices for caring for pregnant women with this condition," Blumer added.

"The guideline synthesizes evidence-based strategies to support women who have diabetes during pregnancy."

Other recommendations from the CPG include:

*All pregnant women who have not previously been diagnosed with diabetes should be tested for gestational diabetes by having an oral glucose tolerance test performed at 24-28 weeks' gestation;*

*Weight loss is recommended prior to pregnancy for women with diabetes who are overweight or obese;*

*Initial treatment of gestational diabetes should be medical nutrition therapy and daily moderate exercise lasting at least 30 minutes;*

*If lifestyle therapy is not sufficient to control gestational diabetes, blood glucose-lowering medication should be added;*

*Women with gestational diabetes should have an oral glucose tolerance test six to 12 weeks after delivery to rule out prediabetes or diabetes;*

*Women who have had gestational diabetes with a previous pregnancy need to be tested for diabetes regularly, especially before any future pregnancies; and*

*Women who have type 1 or type 2 diabetes should undergo a detailed eye exam to check for diabetic retinopathy, and, if damage to the retina is found, have treatment before conceiving.*

The Hormone Health Network has published a fact sheet on gestational diabetes. The resource is available at <http://www.hormone.org/questions-and-answers/2012/gestational-diabetes>.

*Other members of The Endocrine Society task force that developed this CPG include: Eran Hadar of Helen Schneider Hospital for Women in Petach Tikva, Israel; David R. Hadden of Royal Victoria Hospital in Belfast, Northern Ireland; Lois J. Jovanović of Sansum Diabetes Research Institute in Santa Barbara, CA; Jorge H. Mestman of the University of Southern California in Los Angeles; M. Hassan Murad of the Mayo Clinic in Rochester, MN; and Yariv Yogeve of Helen Schneider Hospital for Women.*

[http://www.eurekalert.org/pub\\_releases/2013-11/egu-toi110413.php](http://www.eurekalert.org/pub_releases/2013-11/egu-toi110413.php)

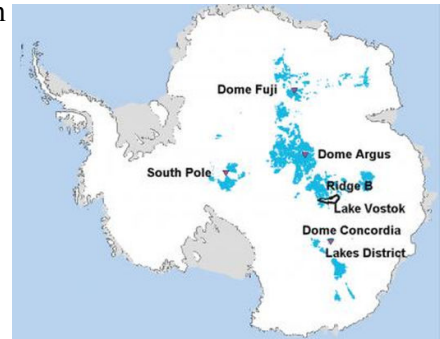
## The oldest ice core

### *Finding a 1.5 million-year record of Earth's climate*

How far into the past can ice-core records go? Scientists have now identified regions in Antarctica they say could store information about Earth's climate and greenhouse gases extending as far back as 1.5 million years, almost twice as old as the oldest ice core drilled to date. The results are published today in *Climate of the Past*, an open access journal of the European Geosciences Union (EGU).

By studying the past climate, scientists can understand better how temperature responds to changes in greenhouse-gas concentrations in the atmosphere. This, in turn, allows them to make better predictions about how climate will change in the future.

"Ice cores contain little air bubbles and, thus, represent the only direct archive of the composition of the past atmosphere," says Hubertus Fischer, an experimental climate physics professor at the University of Bern in Switzerland and lead author of the study. A 3.2-km-long ice core drilled almost a decade ago at Dome Concordia (Dome C) in Antarctica revealed 800,000 years of climate history, showing that greenhouse gases and temperature have mostly moved in lockstep. Now, an international team of scientists wants to know what happened before that.



*This shows Antarctic locations (in bright blue) where 1.5 million years old ice could exist. The figure is modified from Van Liefferinge and Pattyn (*Climate of the Past*, 2013). Credit: Van Liefferinge and Pattyn*

At the root of their quest is a climate transition that marine-sediment studies reveal happened some 1.2 million years to 900,000 years ago. "The Mid Pleistocene Transition is a most important and enigmatic time interval in the more recent climate history of our planet," says Fischer. The Earth's climate naturally varies between times of warming and periods of extreme cooling (ice ages) over thousands of years. Before the transition, the period of variation was about 41 thousand years while afterwards it became 100 thousand years. "The reason for this change is not known."

Climate scientists suspect greenhouse gases played a role in forcing this transition, but they need to drill into the ice to confirm their suspicions. "The information on greenhouse-gas concentrations at that time can only be gained from an Antarctic ice core covering the last 1.5 million years. Such an ice core does not exist yet, but ice of that age should be in principle hidden in the Antarctic ice sheet."

As snow falls and settles on the surface of an ice sheet, it is compacted by the weight of new snow falling on top of it and is transformed into solid glacier ice over thousands of years. The weight of the upper layers of the ice sheet causes the deep ice to spread, causing the annual ice layers to become thinner and thinner with depth. This produces very old ice at depths close to the bedrock.

However, drilling deeper to collect a longer ice core does not necessarily mean finding a core that extends further into the past. "If the ice thickness is too high the old ice at the bottom is getting so warm by geothermal heating that it is melted away," Fischer explains. "This is what happens at Dome C and limits its age to 800,000 years."



To complicate matters further, horizontal movements of the ice above the bedrock can disturb the bottommost ice, causing its annual layers to mix up.

"To constrain the possible locations where such 1.5 million-year old – and in terms of its layering undisturbed – ice could be found in Antarctica, we compiled the available data on climate and ice conditions in the Antarctic and used a simple ice and heat flow model to locate larger areas where such old ice may exist," explains co-author Eric Wolff of the British Antarctic Survey, now at the University of Cambridge.

The team concluded that 1.5 million-year old ice should still exist at the bottom of East Antarctica in regions close to the major Domes, the highest points on the ice sheet, and near the South Pole, as described in the new *Climate of the Past* study. These results confirm those of another study, also recently published in *Climate of the Past*. Crucially, they also found that an ice core extending that far into the past should be between 2.4 and 3-km long, shorter than the 800,000-year-old core drilled in the previous expedition.

The next step is to survey the identified drill sites to measure the ice thickness and temperature at the bottom of the ice sheet before selecting a final drill location. "A deep drilling project in Antarctica could commence within the next 3-5 years," Fischer states. "This time would also be needed to plan the drilling logistically and create the funding for such an exciting large-scale international research project, which would cost around 50 million Euros."

[http://www.eurekalert.org/pub\\_releases/2013-11/nrr-wcb110513.php](http://www.eurekalert.org/pub_releases/2013-11/nrr-wcb110513.php)

### **Why can Buyang Huanwu Decoction be used to treat stroke?**

*Buyang Huanwu Decoction shown to improve the neurological function of patients with stroke*

補陽還五丸

The traditional Chinese medicine Buyang Huanwu Decoction has been shown to improve the neurological function of patients with stroke. Baiyan Liu from Hunan University of Traditional Chinese Medicine, China showed that Buyang Huanwu Decoction significantly increased the number of cells positive for 5-bromodeoxyuridine, a cell proliferation-related marker, microtubule-associated protein-2, a marker of neuronal differentiation, and growth-associated protein 43, a marker of synaptic plasticity in the ischemic rat cerebral regions. The number of positive cells peaked at 14 and 28 days after intragastric administration of Buyang Huanwu Decoction. These findings, published in the *Neural Regeneration Research* (Vol. 8, No. 25, 2013), suggest that Buyang Huanwu Decoction can promote the proliferation and differentiation of neural stem cells and enhance synaptic plasticity in ischemic rat brain tissue.

*Article: "Buyang Huanwu Decoction regulates the neural stem cell behavior in ischemic brain," by Baiyan Liu, Guangxian Cai, Jian Yi, Xuemei Chen (Key Laboratory of Internal Medicine, Hunan University of Traditional Chinese Medicine, Changsha 410007, Hunan Province, China)*

*Liu BY, Cai GX, Yi J, Chen XM. Buyang Huanwu Decoction regulates the neural stem cell behavior in ischemic brain. Neural Regen Res. 2013;8(25):2336-2342.*

[http://www.eurekalert.org/pub\\_releases/2013-11/vcu-dct110513.php](http://www.eurekalert.org/pub_releases/2013-11/vcu-dct110513.php)

### **Drug combination therapy causes cancer cells to 'eat themselves'**

*New drug combination therapy killed colon, liver, lung, kidney, breast and brain cancer cells with little effect on noncancerous cells*

Results from a recent preclinical study have shown that a new drug combination therapy being developed at Virginia Commonwealth University Massey Cancer Center effectively killed colon, liver, lung, kidney, breast and brain cancer cells while having little effect on noncancerous cells. The results lay the foundation for researchers to plan a future phase 1 clinical trial to test the safety of the therapy in a small group of patients. "It is still too premature to estimate when a clinical trial will open to further test this drug combination therapy, but we are now in the planning phase and encouraged by the results of these laboratory experiments," says Andrew Poklepovic, M.D., oncologist and member of the Developmental Therapeutics research program at VCU Massey Cancer Center and assistant professor in the Division of Hematology, Oncology and Palliative Care at VCU School of Medicine. "We are also encouraged by the fact that the drugs used in this therapy are either already approved by the FDA to treat certain cancers or are currently being investigated in other clinical trials."

Featured in the journal *Molecular Pharmacology*, the study led by Paul Dent, Ph.D., demonstrated that the drugs sorafenib and regorafenib synergize with a class of drugs known as PI3K/AKT inhibitors to kill a variety of cancers. Sorafenib and regorafenib work by blocking the production of enzymes called kinases, which are vital to the growth and survival of cancer cells. Sorafenib is currently approved by the FDA to treat kidney and liver cancers, and regorafenib is currently approved for the treatment of colorectal cancer. However, sorafenib and regorafenib do not directly affect PI3K and AKT kinases, which are also very active in promoting cancer cell survival. The addition of a PI3K/AKT inhibitor to the combination of sorafenib and regorafenib

dramatically increased cell death and was even effective against cells with certain mutations that make one or the other drug less effective.

"We know that there are certain cellular processes that are frequently dysregulated in cancers and important to cell proliferation and survival, but if you shut down one, then cells can often compensate by relying on another," says Dent, Universal Corporation Distinguished Professor for Cancer Cell Signaling and member of the Developmental Therapeutics research program at VCU Massey Cancer Center as well as vice chair of the Department of Neurosurgery at VCU School of Medicine. "We are blocking several of these survival pathways, and the cancer cells are literally digesting themselves in an effort to stay alive."

Results of the study showed that the combination therapy killed the cells by physically interacting with molecules to block the survival pathways and induce a toxic effect known as autophagy. Autophagy is a protective process where cells metabolize themselves when starved of the resources needed to survive.

"Many groups are trying the approach of inhibiting two survival signaling pathways, but our approach takes this further by blocking significantly more of these pathways," says Dent. "Our findings could benefit many different cancer patients based on the broad range of effects seen in multiple cancer types."

*In addition to Poklepovic, Dent collaborated on this research with Steven Grant, M.D., Shirley Carter Olsson and Sture Gordon Olsson Chair in Oncology Research, associate director for translational research, co-leader of the Developmental Therapeutics research program and member of the Cancer Cell Signaling research program at VCU Massey; Laurence Booth, Ph.D., Instructor in the Department of Neurosurgery at VCU School of Medicine; Gangadharan B. Sajithlal, Hossein A. Hamed, Ph.D., and Nichola Cruickshanks, Ph.D., all postdoctoral researchers in the Department of Neurosurgery at VCU School of Medicine; and Jahangir Syed, M.D./Ph.D. student in the Department of Biology at VCU.*

*This research was supported by National Cancer Institute grants R01-CA141704 and R01-CA150214, National Institute of Diabetes and Digestive and Kidney Diseases grant R01-DK52825, Department of Defense grant W81XWH-10-1-0009 and, in part, by VCU Massey Cancer Center's NIH-NCI Cancer Center Support Grant P30 CA016059.*

*The full manuscript of this study is available online at: <http://molpharm.aspetjournals.org/content/84/4/562.full>*

[http://www.eurekalert.org/pub\\_releases/2013-11/w-jsp110413.php](http://www.eurekalert.org/pub_releases/2013-11/w-jsp110413.php)

### **Japanese superfood prevents flu infection**

***Scientists have discovered that bacteria found in a traditional Japanese pickle can prevent flu. Could this be the next superfood?***

The research, which assesses the immune-boosting powers of *Lactobacillus brevis* from Suguki – a pickled turnip, popular in Japan – in mice that have been exposed to a flu virus, is published today (06 November) in the SFAM journal, *Letters in Applied Microbiology*. Lead researcher, Ms Naoko Waki of KAGOME CO., LTD. in Japan said: "Our results show that when a particular strain of *Lactobacillus brevis* is eaten by mice, it has protective effects against influenza virus infection."

Suguki enthusiasts have often cited its protective powers but it is not known yet whether the same effects will be seen in humans. Human clinical trials using a probiotic drink containing *Lactobacillus brevis* KB290 bacteria are underway and scientists are hopeful that, given a suitable quantity of bacteria, foods containing them may turn out to be the next superfood. What it is about the bacteria that gives them this amazing property is not known, but it is remarkably tolerant to stomach juices, which are too acidic for many bacteria. This is largely due to a protective layer of sugars called exopolysaccharides.

"We know that exopolysaccharides have immune boosting effects in other similar bacteria, so we wonder if the exopolysaccharides of KB290 are responsible for the effects we see," said Ms Waki. Further studies will be undertaken to investigate this.

The effect of the bacteria is to increase the production of immune system molecules in the body – IFN- $\alpha$  and flu-specific antibodies – and to enhance activity to eradicate virus infected cells. In this study these effects were sufficient to prevent infection by the H1N1 flu and the scientists think that there could also be protection against other viral infections, including the deadly H7N9 flu, which has recently emerged in China.

<http://www.wired.com/wiredscience/2013/11/gut-bacteria-arthritis/>

### **Gut Bacteria May Be Implicated in Rheumatoid Arthritis**

***The bacteria that live in your intestines are a mixed blessing.***

By Beth Skwarecki, ScienceNOW

Scientists have known for decades that this so-called microbiota helps us digest our food and crowds out infectious germs. The bugs have also been implicated in allergies and obesity. Now, a new study adds one more potential malady to the list: rheumatoid arthritis.

"It's been suspected for years and years, both in humans and in the animal model, that the development of autoimmune diseases like arthritis is dependent on the gut microbiota," says immunologist Diane Mathis of Harvard Medical School in Boston. Now, she says, those suspicions are beginning to be confirmed in humans.

"It's a very striking finding."

Rheumatoid arthritis is a mysterious disease. It can strike at any age, typically beginning in young and middle-aged adults and causing painfully stiff, swollen joints in the hands and feet. It can also destroy bone and cartilage and damage organs like the lungs and kidneys.

Scientists aren't sure what causes rheumatoid arthritis, but they do know that it's an autoimmune disorder, meaning that the body's immune system is attacking its own tissues. And that's where gut bacteria come in. Gut bacteria have an intricate relationship with our immune system. We need to be able to tolerate helpful microbes while still recognizing and fighting invaders. Immunologist Dan Littman of New York University knew that gut microbes are important to the development of a particular type of immune cell his team studies, known as a Th17 cell.

Mice that are reared in sterile conditions produce very few of these cells, and his group had previously found that mice bought from one supplier had far more Th17 cells than those that came from a different supplier. The difference turned out to be due to the rodents' gut microbes.

When Littman presented that result at a conference several years ago, Mathis, who was in the audience, told him that she had seen a change in her lab animals when they were moved to a lab in a different town. Instead of spontaneously developing a mouse version of arthritis, they remained healthy. Littman and Mathis collaborated to find out why and tracked down the difference to a particular type of bacterium that, when present in the intestines, trains the immune system to produce Th17 cells, which in turn release molecules that cause inflammation and bone damage in arthritis.

Littman wondered if rheumatoid arthritis in humans might also be due to specific gut microbes. His team tested fecal samples (which reflect the population of gut bacteria) from 114 residents of the New York City area. Some subjects were healthy; others had been living with rheumatoid arthritis for years; still others had psoriatic arthritis, a different autoimmune disease whose causes are also unknown; and some had been recently diagnosed with rheumatoid arthritis

Members of this latter group were especially important because, although they had rheumatoid arthritis, they hadn't yet been treated for it. In this group, a bacterium named *Prevotella copri* was present in 75 percent of patients' intestines, the researchers will report online tomorrow in *eLife*.

*P. copri* only appeared in 37 percent of patients living with either rheumatoid or psoriatic arthritis and 21% of healthy controls. This last number is similar to the prevalence of *P. copri* that previous studies found in the general population in industrialized countries.

"That they were able to associate one bacterium with one pathology is remarkable," says Yasmine Belkaid, an immunologist at the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland, who was not involved in the work.

But the results aren't enough to convict *P. copri* as the mastermind behind rheumatoid arthritis, she notes. The authors can't ethically give the bacterium to healthy subjects, so they couldn't prove that *P. copri* caused arthritis in patients, just that the bacterium and the disease tend to occur together.

Genetics and other environmental factors, like smoking, have been associated with rheumatoid arthritis, so even if *P. copri* is the culprit, it doesn't necessarily act alone. "The next step is to be able to understand how causative these microbes are," Belkaid says. That would require surveying people's microbes and waiting to see who develops the disease.

To build its case against the bacterium, Littman's team gave a lab-grown strain of *P. copri* to mice and watched what happened in the rodents' guts. *P. copri* easily took up residence, and the researchers found that the mice developed increased inflammation, especially in the gut.

They didn't get arthritis, possibly because the strain of *P. copri* was different from the human ones, but Littman says the gut inflammation corroborates the idea that gut microbes are prodding immune cells to develop and that those cells then go forth and lead an attack on other parts of the body.

That is the most exciting possibility, Mathis says. But, she explains, other hypotheses can't be ruled out. It's possible that arthritis patients' immune systems allow *P. copri* to grow out of control, or perhaps a third factor affects both the microbes and the immune system independently. Rheumatoid arthritis, Littman says, seems to have several environmental triggers, but how and whether they combine is not well understood.

The findings, Mathis says, open the possibility of new therapies to prevent or treat rheumatoid arthritis. Current treatments for the disease include drugs with scary side effects - Remicade, for instance, seems to increase the risk of developing certain cancers and serious infections. Perhaps *P. copri* could be attacked with antibiotics, Littman says, or crowded out with probiotic pills full of good bacteria. Either way, patients may someday be able to relieve their joint pain by focusing on their guts.

<http://www.bbc.co.uk/news/science-environment-24820279>

## Physicists probe urination 'splashback' problem

*US physicists have studied the fluid dynamics of urine "splashback" - and found tips to help men and women with their accuracy and hygiene.*

By James Morgan Science reporter, BBC News

Using high-speed cameras, the team filmed jets of liquid striking toilet walls and studied the resulting spray. Splashback was low when the jets were used close up with a narrow "angle of attack", said the Brigham Young University team. They will present their research at an American Physical Society meeting.

"In response to harsh and repeated criticisms from our mothers and several failed relationships with women, we present the splash dynamics of a simulated human male urine stream," reads their conference abstract.

But there is a more serious side to the research.

The work is led by Prof Tadd Truscott and Randy Hurd of the "Splash Lab" at Brigham Young in Provo, Utah, who jokingly refer to themselves as "wizz kids". "People ask me, are you serious? I tell them yes, this may involve 12-year-old humour, but it's also a real problem," Prof Truscott told BBC News. "We've all been in disgusting toilets with puddles on the floor - these places are a breeding ground for bacteria."

For example, the detergents used to clean hospital toilets could actually increase the spray of disease-causing bacteria, by reducing the surface tension of water, according to a recent study.

One might think the physics of aiming urination had already been summarised by the formula: "get it all in the bowl". But micturation is still a messier business than it needs to be, according to the research.

Taking measurements live "in the field" did not appeal to the scientists, so the duo built a urination simulator. The "Water Angle Navigation Guide" is a five-gallon bucket with hoses connected to two types of synthetic urethra.

### Chaotic spray

The team fired coloured water at various target "toilets" at the velocity and pressure of average human urination. Then, using a high-speed camera, they captured the moment of impact in remarkable visual detail.

Splashback was heightened by a phenomenon known as Plateau-Rayleigh instability, where a falling stream of liquid breaks up into droplets. "The male urine stream breaks up about 6-7 inches outside the urethra exit," Mr Hurd explained. "So by the time it hits the urinal, it's already in droplet form. And these droplets are the perpetrators of the splash formation on your khaki pants." His advice? "The closer you are, the better. If you can get stream impact with the porcelain, it's a lot less chaotic."

Of course, in a domestic bathroom, distance from the toilet is governed chiefly by one variable: "to stand or sit". "People are always arguing over which is better. Because when you sit close, you're also closer to getting wet," said Prof Truscott.

"In Germany there is a derogatory term 'sitzpinkler' for a man who sits down to pee. It means he's kind of a wuss. "So we wanted to look at whether sitting down is really effective. What are the splash differences?"

To compare the two positions, the scientists gave rulers to their friends and sent them into the toilet.

"It turns out you are five times as far away when you stand up - and that's a pretty significant difference in impact velocity for those droplets of urine," said Mr Hurd.

Impact with the toilet water is captured in a video by the team. "You can see the droplets create a large cavity in the water, which then collapses, causing even greater splashback. The amount of splash is considerable," Mr Hurd explained. "It seems that sitting down is the best sure-fire way to avoid unwanted splashing in a traditional toilet."

### Angle of attack

Above all, he says, "the biggest thing you can do" to reduce splashback - sitting or standing - is to alter the "angle of attack". Aiming directly at a vertical urinal wall - a 90 degree angle - causes a nasty kickback, as does aiming directly at the toilet water. "Narrowing the angle really helps," said Mr Hurd. For a typical urinal, "best practice" means standing slightly to one side, and aiming downwards at a low angle of impact. "This way you take advantage of both splash-reduction techniques," Hurd explains.

Prof Truscott encourages men and women to "be artistic" with their aim and find an angle to suit the particular facility they are faced with.

The designs of public toilets and home bathrooms does not always help us achieve 100% efficiency, he said. "Most surfaces you pee into, such as porcelain, are hydrophilic, which is a disadvantage. The water spreads across them, creating a puddle to splash into," said Mr Hurd. He believes that hydrophobic coatings will ultimately make toilets more hygienic, with important benefits for hospitals, schools, and workplaces.

The Brigham-Young team has been "inundated" with commercial products to reduce spray - such as fabric inserts, urinals with triangular fins, and toilet bowls with unusually sloping angles.



"Some work fantastically - others really don't work at all. It's almost worse than nothing," says Truscott.

"My favourite is painting a fly on the wall to indicate where you should aim. Unfortunately, some companies put that fly in the wrong place." Sega has even developed a "Toylet" urinal game, installed in Tokyo Metro stations to award men points for accuracy. But Prof Truscott says one of the most effective tricks is also the simplest - drop a few pieces of tissue into a toilet bowl to soften the blow.

The Splash Lab team plans to investigate further toilet designs and find "the optimal approach for urinal usage", removing some of the obstacles between men, women and bathroom harmony.

<http://www.newyorker.com/online/blogs/elements/2013/11/do-our-bones-influence-our-minds.html>

## Do Our Bones Influence Our Minds?

*In the mid-nineteen-nineties, a young French geneticist and physician named Gerard Karsenty became curious about a mysterious protein, called osteocalcin, that is found at high concentrations in the skeleton.*

Posted by Amanda Schaffer

He worked with mice that had been engineered to lack the substance, expecting to find problems with their bones. But their skeletons appeared essentially normal, he says, a result that left him "deeply depressed."

The mice did have issues, though. Their abdomens were fatty, they had trouble breeding, and they were "stupid," meaning "they never rebelled or tried to bite or escape," said Karsenty, now fifty-nine years old and the chair of the department of genetics and development at Columbia University Medical Center. He has studied osteocalcin for almost two decades. While its role within the skeleton remains unknown, he has shown that the substance has wide-ranging effects on mice's fat stores, livers, muscles, pancreases, testes, and even, as new evidence suggests, their brains. It turns out that osteocalcin is a messenger, sent by bone to regulate crucial processes all over the body.

The finding represents new ground in how researchers view the skeleton: not only do bones provide structural support and serve as a repository for calcium and phosphate, they issue commands to far-flung cells. In mice at least, they talk directly to the brain. "This is a biggie," said Eric Kandel, the neuroscientist and Nobel Laureate. "Who thinks of the bone as being an endocrine organ? You think of the adrenal gland, you think of the pituitary, you don't think of bone."

But Karsenty has long believed that our skeletons do a lot more than just give our bodies their shape. In 2007, he suggested that bones play a crucial role in regulating blood sugar: mice engineered to lack osteocalcin were essentially diabetic; they were less sensitive to insulin, and produced less of it. When he provided osteocalcin, however, their insulin sensitivity and blood sugar normalized. When Karsenty first presented these findings at a conference, endocrine experts were "overwhelmed by the potential implications," as one of them told me at the time.

Similarly, Karsenty has raised provocative questions about the skeleton's role in fertility. In 2011, he showed that bones play a crucial role in male reproduction: mice that did not produce osteocalcin had abnormally low levels of testosterone and were sterile. Mice that produced high levels, on the other hand, had more testosterone and bred more frequently. (The mechanism did not appear to be relevant to females.)

The most recent finding concerns the skeleton and the brain. In a paper published in late September in the journal *Cell*, Karsenty showed that bone plays a direct role in memory and mood. Mice whose skeletons did not produce osteocalcin as a result of genetic manipulation were anxious, depressed, and almost completely unable to master a test of spatial memory. When Karsenty infused them with the missing hormone, however, their moods improved and their performance on the memory test became nearly normal. He also found that, in pregnant mice, osteocalcin from the mother's bones crossed the placenta and helped shape the development of the fetus's brain. In other words, bones talk to neurons even before birth.

What might this chatter mean for human health? As we age, our bone mass decreases. Memory loss, anxiety, and depression also become more common. These may be separate, unfortunate facts about getting old, but they could also be related. "If you ask physicians the best things to do to prevent age-related memory loss, they'll say exercise," Kandel points out. Does exercise help partly because it works to maintain bones, which make osteocalcin, which in turn helps preserve memory and mood? (Karsenty speculates that a higher bone mass means a greater capacity for osteocalcin production, though this has yet to be established.) Even more fantastically: Would it ever be possible to protect memory or treat age-related cognitive decline with a skeletal hormone? These are the kinds of questions that can spur either false hopes or imaginative leaps.

Karsenty's vision of the skeleton as central to energy usage, reproduction, and memory has persuasive evidence in mice. If one of these studies "had come in isolation, I think I would have more skepticism toward it," Sundeep Khosla, of the Mayo Clinic, said. But they're "part of a whole series showing that bone helps regulate other tissues, and the findings in mice are well done and compelling." (Much of the earlier work has also been corroborated by other labs, also using mouse models.)

The question has always been the extent to which these results translate to people. "I don't know of any hormone that functions in mice but not to some extent in humans," Thomas Clemens, of Johns Hopkins, told me in 2011. Still, osteocalcin is clearly not the only substance that regulates blood sugar or male fertility or cognition, and its relative importance may be different in people. In mice, no other substance can compensate for a lack of osteocalcin when it comes to these functions, as Karsenty's work shows. Is the same true in humans?

One tantalizing hint comes from men who are unable to respond to the hormone as a result of a genetic mutation. Karsenty has identified two such men, and they are both infertile and unable to regulate sugar normally - what the mouse models would predict. The real test, however, would be a clinical trial in which researchers identified patients with a genetic defect related to osteocalcin - or patients with low levels of osteocalcin, perhaps as a result of declining bone mass - and treated them with the hormone to see whether it reversed low fertility, poor memory, anxiety, or depression.

Karsenty also believes that we know enough now to recognize that the body is far more networked and interconnected than most people think. "No organ is an island," he likes to say. And if X talks to Y, then Y should talk back to X. This insistence on reciprocity has animated much of his career, with the skeleton often playing a surprise role: insulin acts on bone, and bone should help regulate insulin. Testosterone has an influence on bone mass, and the skeleton should act on the testes. And just as the brain talks to the skeleton, he says, "I always knew that bone should help regulate the brain. I just didn't know how."

[http://www.eurekalert.org/pub\\_releases/2013-11/uow-fdp110113.php](http://www.eurekalert.org/pub_releases/2013-11/uow-fdp110113.php)

### **Floods didn't provide nitrogen 'fix' for earliest crops in frigid North**

*Floods didn't make floodplains fertile during the dawn of human agriculture in the Earth's far north because the waters were virtually devoid of nitrogen, unlike other areas of the globe scientists have studied.* Instead, the hardy Norsemen and early inhabitants of Russia and Canada have microorganisms called cyanobacteria to mostly thank for abundant grasses that attracted game to hunt and then provided fodder once cattle were domesticated. The process is still underway in the region's pristine floodplains.

The new findings are surprising because it's long been assumed that nitrogen crucial to plant growth mainly arrived with floods of river water each spring, according to Thomas DeLuca, a University of Washington professor of environmental and forest sciences and lead author of a paper in the Nov. 6, 2013 issue of the journal PLOS ONE.

Discovering that cyanobacteria in the floodplains were responsible for nitrogen fixation – that is taking it from the atmosphere and "fixing" it into a form plants can use – partially resolves the scientific debate of how humans harvested grasses there for hundreds of years without fertilizing, DeLuca said.

It raises the question of whether farmers today might reduce fertilizer use by taking advantage of cyanobacteria that occur, not just in the floodplains studied, but in soils around the world, he said.

It also might lead to more accurate models of nitrogen in river systems because none of the prominent models consider nitrogen being fixed in floodplains, DeLuca said.

Scientists model nitrogen loading of rivers, especially where industrial fertilizers and effluent from wastewater-treatment plants cause dead zones and other problems in the lower reaches and mouths of rivers.

Ten rivers and 71 flood plains were studied in northern Fennoscandia, a region that includes parts of Scandinavia and Finland. The rivers were chosen because their upper reaches are pristine, haven't been dammed and are not subject to sources of human-caused nitrogen enrichment – much like river systems humans encountered there hundreds of years ago, as agriculture emerged in such "boreal" habitats.

Boreal habitat – found at 60 degrees latitude and north all the way into the Arctic Circle, where it meets tundra habitat – is the second largest biome or habitat type on Earth.

In the northern regions of the boreal, the surrounding hillsides have thin, infertile soils and lack shrubs or herbs that can fix nitrogen. In these uplands, feather mosses create a microhabitat for cyanobacteria, which fix a modest amount of nitrogen that mostly stays on site in soils, trees and shrubs.

Little of it reaches waterways. On the floodplains, high rates of nitrogen fixation occur in thick slimy black mats of cyanobacteria growing in seasonably submerged sediments and coating the exposed roots and stems of willows and sedges.

"We joke and call the floodplains the 'mangroves of the North' because there are almost impenetrable tangles of willow tree roots in places, like a micro version of the tropical and subtropical mangroves that are known to harbor highly active colonies of cyanobacteria," DeLuca said. "It turns out there's a lot of nitrogen fixation going on in both," he said. For example, the scientists discovered that in spite of the dark, cold, snowy winters of Northern Sweden, the cyanobacteria there fix nitrogen at rates similar to those living the life in the toasty,

sun-warmed Florida Everglades. The amount of nitrogen provided by the cyanobacteria to unharvested willows and sedges is perhaps a quarter of what U.S. farmers in the Midwest apply in industrial fertilizers to grain crops and as little as a sixth of what they apply to corn.

Human-made fertilizers can be fuel-intensive to produce and use, for example, it takes the energy of about a gallon of diesel to produce 4 pounds of nitrogen fertilizer. In developing countries in particular, nitrogen fertilization rates are spiraling upward, driving up fossil-fuel consumption, DeLuca said.

Meanwhile, cyanobacteria naturally occurring in farm soils aren't fixing nitrogen at all in the presence of all that fertilizer, they just don't expend the energy when nitrogen is so readily available, he said.

"Although modest in comparison to modern fertilization, the observation that cyanobacteria could drive the productivity of these boreal floodplain systems so effectively for so long makes one question whether cyanobacteria could be used to maintain the productivity of agricultural systems, without large synthetic nitrogen fertilizer inputs," he said.

*Co-authors on the paper are Olle Zackrisson and Ingela Bergman with the Institute for Subarctic Landscape Research, Sweden, Beatriz Díez with Pontificia Universidad Católica, Chile, and Birgitta Bergman with Stockholm University.*

*Funding for the work came from the European Regional Development Fund and the Bank of Sweden Tercentenary Foundation.*

[http://www.eurekalert.org/pub\\_releases/2013-11/uom-msf110613.php](http://www.eurekalert.org/pub_releases/2013-11/uom-msf110613.php)

### **MU study finds more accurate method to diagnose pancreatic cancer**

***Researchers from the University of Missouri have found a more accurate laboratory method for diagnosing pancreatic cancer, the fourth leading cause of cancer death in the United States.***

COLUMBIA, Mo. - The disease causes more than 38,000 deaths each year in the United States, and kills 94 percent of people with the illness within five years, according to the National Cancer Institute.

"Pancreatic cancer can be difficult to diagnose because of subtle differences that distinguish between healthy tissue, cancerous tissue and tissue that is atypical, or suspicious," said Lester Layfield, M.D., professor and chair of the MU School of Medicine's Department of Pathology and Anatomical Sciences.

"Our goal was to find a way to make a more accurate and reproducible diagnosis."

Because of the pancreas' location within the body, no routine screening methods, such as mammography for breast cancer, exist for detecting pancreatic cancer.

If a physician suspects a patient may have pancreatic cancer, a biopsy of the pancreatic tissue is taken through a minimally invasive technique called endoscopic ultrasound-guided fine-needle aspiration.

"Traditionally, pathologists have examined a tissue sample through a microscope and made a diagnosis based on the overall features of all the cells in the tissue sample," Layfield said. "Previous research has shown an experienced pathologist can diagnose pancreatic cancer with accuracy in the mid-to-upper 80 percent range using current techniques. However, we wanted to develop a more accurate method by determining which cellular features are most closely associated with cancer."

To develop the new diagnostic method, MU researchers performed a retrospective study of the records from 57 patients at University of Missouri Health Care who were tested for pancreatic cancer. They evaluated 16 features of pancreatic biopsies that could be evaluated under a microscope and performed a statistical analysis to determine which could be most reliably identified by multiple pathologists and which were most likely to be associated with pancreatic cancer.

"Through our analysis, we developed a group of four characteristics that allow a pathologist to diagnose pancreatic cancer with 93 percent accuracy - a substantial improvement over the traditional method," Layfield said. "I believe this new technique can help pathologists improve the diagnosis of pancreatic cancer, ultimately improving care for patients by providing an evidence-based approach to diagnosing the disease and determining the best treatment." The four features of pancreatic cancer the researchers identified are:

*a wide variation in the size of pancreatic cells' nuclei, called anisonucleosis*

*oversized nucleoli, called macronucleoli*

*single atypical epithelia cells, a type of cell found in the pancreas*

*mucinous metaplasia, which is the production of mucin in cells that normally don't produce the substance*

*The study, "Risk Stratification Using Morphological Features in Endoscopic-ultrasonography Guided Fine Needle Aspirations of Pancreatic Ductal Adenocarcinoma," was presented at the American Society for Clinical Pathology's 2013 annual meeting.*

<http://www.sciencedaily.com/releases/2013/11/131106101519.htm>

### **New Antifungal Composition Effectively Inhibits Wide Variety of Fungi**

***In order to overcome resistance to antifungal variety of pathogenic fungi and yeast, researchers from the University of Alicante have developed a novel and efficient antifungal composition with pharmacological applications in agriculture and food industry, among others.***

The composition, developed and patented by the UA Research Group in Plant Pathology, is based on the combined use of chitosan, or chitosan oligosaccharides (COS), antifungal agents and additives that synergistically affect the growth of a variety of pathogenic fungi.

"Chitosan is a non-toxic biopolymer, biocompatible and naturally degradable, with antibacterial, antiviral and antifungal properties obtained from chitin, the main constituent of hard body parts of invertebrates, such as the shells of shrimp, lobsters, crabs, and other marine crustaceans, and is part of the fungal cell wall," as explained by lecturer Luis Vicente López Llorca, Director of the UA Research Group in Plant Pathology and head of the research work.

"Because many fungal pathogens develop resistance to prolonged treatment with antifungal drugs, it is desirable to find alternatives for their control in medical, agricultural and those applications in which the fungi cause damage. In clinics, pathogenic fungi resistant to antifungal drugs are a major cause of mortality in patients. Chitosan and the antifungal additives, some based on the identification of molecular targets of chitosan, contribute to produce a novel alternative to control fungal diseases and in particular antifungal resistant strains" López Llorca said.

The various experiments carried out by the research group are proof of the significant synergistic effect of the combination of chitosan (or COS) and other antifungals and ARL1 gene inhibitor, in inhibiting the growth of mold and yeast. "Chitosan is nontoxic to mammals, making it suitable for use as an antifungal in various applications," Luis Vicente López adds.

"The chitosan or COS and a joint inhibition of some of its gene targets block the cell cycle and transcription in yeast, leading to oxidative stress, cell death and growth inhibition" López Llorca indicates. In this regard, the combination may have potential in the treatment of tumors.

This novel composition can be used as a medicine for clinical or veterinary use for the treatment and/or prevention of fungal infections by pathogenic yeasts and filamentous fungi, such as *Candida* spp. *Cryptococcus* spp., *Fusarium* spp. and probably also in the control of tumor cells. In agriculture, pesticide treatments, preferably in the control of diseases caused by pathogenic fungi as *Botrytis cinerea* and *Fusarium oxysporum*. In the food industry, for example, for coating foods to prevent microbial contamination, and in the textile industry, as a detergent for cleaning surfaces.

The research group has led numerous laboratory tests that have successfully proven the effectiveness of this novel composition of fungal growth inhibition of numerous species of pathogenic yeasts and filamentous fungi. The industrial scale is simple and economically viable compared to the benefits of this invention in the various fields of application.

[http://www.eurekalert.org/pub\\_releases/2013-11/cu-moo110613.php](http://www.eurekalert.org/pub_releases/2013-11/cu-moo110613.php)

### **Movin' on out**

#### ***Support of parents and peers vital for millennials leaving home: New study from Concordia University***

Leaving home is an important milestone that signals entry into adulthood. But young people are staying home longer than ever before. In fact, the 2011 census report from Statistics Canada shows that 42.3 per cent of young adults aged 20 to 29 still lived with their parents - that's compared to 32.1 per cent in 1991, and 26.9 per cent in 1981.

The diminishing number of blue-collar jobs, rising costs of housing and increasing need for prolonged postsecondary education have impacted how, when and why young adults leave home. At the same time, youth today are less driven to take on adult responsibilities than previous generations.

Recent research shows that individuals in their early 20s - also known as millennials - undergo a brand-new life stage not experienced by previous generations: emerging adulthood. A new study from Concordia's Department of Applied Human Sciences examines how moving out on one's own is a critical element in the transition to adulthood.

It turns out that moving out represents a significant transition that can constitute a crisis. Luckily, this crisis can be overcome with a little help from friends and family, a finding that also has implications for disadvantaged youth.

Varda Mann-Feder, a professor in the Department of Applied Human Sciences and first author of the forthcoming study in the *Canadian Journal of Family and Youth*, explains that parents and peers are deeply implicated in the moving-out process. This was confirmed by the in-depth interviews that she and her research team conducted with 32 emerging adults who had either left home or were contemplating such a move. Study participants who had already left home said that parents made significant contributions to a successful move, both through pragmatic help and the provision of an emotional and financial safety net. Peers were



equally important, as participants preferred to turn to friends, rather than to their parents, to learn the skills needed for autonomous living.

For those participants still at home, peers and parents were seen as extremely influential in relation to ideas about leaving the proverbial nest. Peers who had already left home represented a key source of information about moving out, and about whether or not to do it. The ability to observe peers and adopt similar strategies or avoid their mistakes also provided reassurance for participants at home.

"This study shows peers continue to play a critical role in development after the teenage years," says Mann-Feder. "They provide unique input not available from parents or romantic partners. This finding gives me hope for those emerging adults who do not have the benefit of a parental safety net; that is, for individuals forced to transition out of foster care, mental health institutions or juvenile justice situations when they reach the age of majority."

She notes that, despite large investments in programs for transitioning these youth into independent living, outcomes have been poor overall. Mann-Feder intends this study to be the first step in a program of research that will help design targeted programs and policies supporting healthy transitions to adulthood for disadvantaged youth.

**Research in action:** Concordia's new Graduate Diploma in Youth Work will further this type of research. The 33-credit program prepares students for work with youth in both the regular community as well as in specialized contexts like foster care. The applied approach of this diploma integrates community youth development with clinical work.

Says Mann-Feder: "Our students will develop advanced intervention skills, the ability to establish facilitative relationships and use collaborative strength-based approaches in a range of contexts."

*Partners in research:* This research was made possible by funding from the Social Sciences and Humanities Research Council of Canada. The study was co-authored by Allison Eades and Emma Sobel, graduate students in Concordia's Human Systems Intervention program, as well as Jack DeStefano from McGill University.

[http://www.eurekalert.org/pub\\_releases/2013-11/pc-nrs110613.php](http://www.eurekalert.org/pub_releases/2013-11/pc-nrs110613.php)

## **New research shows tea may help promote weight loss, improve heart health and slow progression of prostate cancer**

*American Journal of Clinical Nutrition releases new proceedings from International Tea and Human Health Symposium*

New York, NY : Decades worth of research shows that tea - the second most consumed beverage in the world - may help prevent chronic illnesses, including heart disease, certain types of cancer and type 2 diabetes. New research shows tea has been found to help promote weight loss and maintain a healthy weight, improve bone health and activate areas of the brain that bolster attention, problem solving and mood.

The December 2013 issue of the American Journal of Clinical Nutrition features 12 new articles about the relationship between tea and human health. Each paper is based on presentations from world-renowned scientists who participated in the Fifth International Scientific Symposium on Tea and Human Health, held at USDA in September 2012. Highlights of some of the compelling reports published through the AJCN include the following five papers:

### **Tea Leaf Polyphenols May Promote Weight Loss**

Tea polyphenols and the caffeine content in tea increase energy expenditure and fat oxidation, providing benefits for achieving and maintaining an ideal body weight. The results of one meta-analysis suggests the increase in caloric expenditure is equal to about 100 calories over a 24-hour period, or 0.13 calories per mg catechins. In a related review, researchers concluded that subjects consuming green tea and caffeine lost an average of 2.9 pounds within 12 weeks while adhering to their regular diet. Population-based studies also show that habitual tea drinkers have lower Body Mass Indexes (BMIs) and waist-to-hip ratios and less body fat than non-tea drinkers. In addition, green tea and caffeine also appear to boost fat oxidation over 24 hours by an average of 16% or 0.02 grams per mg catechins.

### **Tea May Reduce Risk for Some Cancers**

Green tea polyphenols may play a role in arresting the progression of certain cancers. For example, in a double-blind, placebo-controlled study, supplementation with 600 mg/d green tea catechins reduced the progression of prostate cancer. The researchers reported that after a year, 9% of men in the green tea supplemented group had progressed to prostate cancer whereas 30% of men in the placebo group had progressed.

Hundreds - if not thousands - of laboratory, epidemiological and human intervention studies have found anti-cancer properties in compounds present in tea. The types of cancer that have shown benefits of tea include cancers of the gastrointestinal tract, lung, prostate, breast, and skin. The proposed mechanisms of action for

providing protection against cancer include antioxidant effects, inhibition of growth factor signaling, as well as improving the efficacy of chemotherapy agents.

### **Tea Catechins are Cardioprotective**

Numerous studies suggest tea supports heart health and healthy blood pressure, and appears to be associated with a reduced risk of cardiovascular disease, including stroke and heart attack. New research, published in the AJCN provides further support. Study results published by Claudio Ferri, MD, University L'Aquila, Italy, found that black tea reduced blood pressure, and among hypertensive subjects, it helped counteract the negative effects of a high-fat meal on blood pressure and arterial blood flow. Hypertensive subjects were instructed to drink a cup of tea after a meal that contained 0.45 grams fat/lb. body weight. The results suggest that tea prevented the reduction in flow-mediated dilation (FMD), the ability to increase arterial blood flow that occurs after a high-fat meal. In a previous study conducted by Ferri, tea improved FMD from 7.8 to 10.3%, and reduced both systolic and diastolic blood pressure by -2.6 and -2.2 mmHg, respectively, in study participants. "Our studies build on previous work to clearly show that drinking as little as one cup of tea per day supports healthy arterial function and blood pressure. These results suggest that on a population scale, drinking tea could help reduce significantly the incidence of stroke, heart attack and other cardiovascular diseases," concluded Dr. Ferri.

### **Tea Flavonoids Improve Bone Strength and Quality**

Osteoporosis is a major public health concern but new research suggests that polyphenols in green tea may help improve bone quality and strength through many proposed mechanisms. In fact, one study found that tea drinking was associated with a 30% reduced risk in hip fractures among men and women over 50 years old. In a study of 150 postmenopausal women, researchers reported that 500 mg green tea extract (equivalent to 4-6 cups of green tea daily), alone or in combination with Tai Chi, improved markers for bone formation, reduced markers of inflammation and increased muscle strength in study participants. Numerous other studies have found that green tea flavanols provide a restorative effect to bone remodeling to help maintain bone density and slow bone loss.

### **Tea Improves Mood, Alertness and Problem Solving**

Results from new research published in the American Journal of Clinical Nutrition found that drinking tea improved attention and allowed individuals to be more focused on the task at hand. In this placebo-controlled study, subjects who drank tea produced more accurate results during an attention task and also felt more alert than subjects drinking a placebo. These effects were found for 2-3 cups of tea consumed within a time period of up to 90 minutes. Several studies have evaluated the role of tea in strengthening attention, mood and performance, and the results have been promising. It is thought that the amino acid theanine and caffeine, both present in tea, contribute to many of tea's psychological benefits.

Twelve internationally renowned researchers contributed to the AJCN supplement, including experts from USDA, National Institutes of Health, UCLA, University of Glasgow and University of L'Aquila, among others. "The scientists who contributed their original research and insights are among the best in the world, and together, this body of research has significantly advanced the science of tea and human health," said compendium editor Jeffrey Blumberg, PhD, Professor, Friedman School of Nutrition Science and Policy and Director, Antioxidants Research Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Boston.

"These new peer-reviewed papers add to the previously-published body of evidence that shows that tea can improve human health - both physically and psychologically," added Blumberg. "Humans have been drinking tea for some 5,000 years, dating back to the Paleolithic period. Modern research is providing the proof that there are real health benefits to gain from enjoying this ancient beverage."

AJCN published 12 new articles on the relationship between tea and human health including:

*Tea consumption and cardiovascular disease risk*

*Human studies on the absorption, distribution, metabolism, and excretion of tea polyphenols*

*Tea, flavonoids, and cardiovascular health: endothelial protection*

*Acute effects of tea consumption on attention and mood*

*Cancer prevention by green tea: evidence from epidemiologic studies*

*Catechin- and caffeine-rich teas for control of body weight in humans*

*Tea and flavonoids: where we are, where to go next*

*Cellular targets for the beneficial actions of tea polyphenols*

*Does tea prevent cancer? Evidence from laboratory and human intervention studies*

*Tea and bone health: steps forward in translational nutrition*

*Interactions of black tea polyphenols with human gut microbiota: implications for gut and cardiovascular health*

<http://www.sciencedaily.com/releases/2013/11/131106122117.htm>

## Don't Get Sick in July

*With almost no experience, newly graduated medical students enter teaching hospitals around the country every July, beginning their careers as interns. At the same time, the last year's interns and junior residents take a step up and assume new responsibilities.*

In addition to developing their nascent clinical skills, each entering class of interns must grasp the many rules and standards for operating in this "new" hospital structure.

More experienced physicians share a joke about this changing of the guard: Don't get sick in July.

But the data to back up this quip has proven hard to find. Over the years, numerous studies have shown no effect or very slight effects when comparing patient outcomes in July versus the preceding May, when trainees are more experienced and concluding their training cycles. Some researchers have suggested that the safeguards academic medical centers put in place, such as increased supervision by more experienced doctors during this first phase in the training cycle, protect patients from the effects of inexperience and organizational disruption. A new study published Oct. 23 in *Circulation* by researchers at Harvard Medical School, Stanford University Hospitals, University of Southern California and the RAND Corporation, has found that while the so-called "July effect" is negligible in most cases, it is a serious concern for high-risk patients.

"The good news for patients is that in most cases, it's very difficult for a physician to make a mistake that results in a patient's death," said Anupam Jena, HMS assistant professor of health care policy and of medicine at Massachusetts General Hospital and lead author of the study. "But for severely ill patients, health can be very tenuous. A small error or a very slight delay in care is potentially devastating."

Jena and colleagues analyzed cases from more than 1,400 hospitals using data from the U.S. Nationwide Inpatient Sample. They compared patients who came to teaching and non-teaching hospitals with acute myocardial infarctions, commonly known as heart attacks. The researchers separated cases into low-risk and high-risk categories and compared outcomes.

Overall, they found that patients at teaching hospitals had a lower risk of dying than at non-teaching hospitals, but in July, the risk at teaching hospitals rose to the same level that patients at non-teaching hospitals faced. For high-risk patients who came to the teaching hospitals with heart attacks, the risk of death in hospital went from 20 percent to 25 percent. They also found that among teaching hospitals, the difference between outcomes in May and July is greatest in institutions with the highest percentages of trainees.

The researchers ruled out two potential factors that they suspected may have accounted for some of that difference -- the prevalence of percutaneous coronary intervention (i.e. cardiac stents) and of complications from the use of blood thinners.

Without evidence for specific procedures or protocols that could prevent increased deaths, the researchers said that their findings suggest that, especially during the early months in the training cycle, oversight should be intensively focused on high-risk cases rather than across cases overall. In July, doctors with more experience should play a greater role in the care of high-risk patients than has typically been the case. "Teaching hospitals should revisit what steps are needed to safely and effectively care for high-risk patients in July," Jena said.

*A. B. Jena, E. C. Sun, J. A. Romley. Mortality among High Risk Patients with Acute Myocardial Infarction Admitted to U.S. Teaching-Intensive Hospitals in July: A Retrospective Observational Study. Circulation, 2013; DOI: 10.1161/CIRCULATIONAHA.113.004074*

<http://www.wired.com/wiredscience/2013/11/wired-data-life-theranos/>

## What Health Care Needs Is a Real-Time Snapshot of You

*Healthcare can be a very slow-moving beast. Getting something as seemingly easy as a basic metabolic panel or an HIV test done can take days.*

By Daniela Hernandez

First, your blood is drawn, then it's sent to a lab where your samples are actually processed. The lab does the tests your doctor ordered and days later they send her back the results.

That's a problem because while the lab was working its slow magic, your body was changing.

"How long can I expect that to still represent me?" said Atul Butte, a professor of pediatrics at Stanford University. "That's a hard problem and not an easy one to figure out. We're not static. We're constantly aging and changing. It's really hard to think about changes across time."

Faster turnaround and more frequent and coordinated testing could be a first step toward solving that issue.

Recently, diagnostics company Therasanos opened its first "wellness center" in a Walgreens drug store a few miles away from its Palo Alto, California headquarters to help make this happen. For the last 10 years, the company has been developing new chemistry and technologies that could make it possible to do the same clinical laboratory tests as services like Quest Diagnostics, but much more quickly, cheaply and with about one

thousandth the volume of blood that's normally taken from patients. The small volume, paired with a fast turnaround time, is the key. Because the technique requires such tiny volumes, patients can give blood samples more often, which could help doctors track patients' health better in a closer to real-time fashion. Getting your blood drawn by Theranos doesn't require needles, large vials, or tubing. A phlebotomist pricks your finger with a needle that feeds a tiny volume of blood into a 0.5-inch long "nanotainer." That teensy vial is then placed in a box until your "microsample" is processed. The results from testing are beamed back to the patient and her doctor over the internet in just a few hours.

"Theranos was founded with the goal of making actionable health information accessible to people everywhere at the time it matters most," said CEO Elizabeth Holmes today at the WIRED Data | Life conference in New York. The company is trying to create tools for physicians to be able to track data better overtime. This type of information, she says, could be used to provide more nuanced insights into where people's health is headed. But that is still only a snapshot. Other health information, like a patient's x-rays, electrocardiograms, or PET scans, are unlikely to be time-matched to the tests Theranos runs. Theranos data can be integrated into electronic medical records, but data patients collect about themselves in apps still live in silos that can't be easily integrated into analog or electronic medical records.

"Fragmentation [in healthcare] is still quite severe," said Murray Aitken, the executive director of the IMS Institute for Healthcare Informatics. "It really does reduce the ability to understand fully the state of health of the patient and how they can be treated. Just having all the information in one place for the patient at one time would be a huge step forward."

To make all this data more valuable to doctors and patients, better integration and methods for collecting data will likely need to be developed - and that's unlikely to result from the efforts of a single Silicon Valley startup. The company's emphasis on miniaturization and speed has garnered a lot of attention, but some don't think it's necessarily ground-breaking.

"Doing tests from small blood samples is interesting, but I'm not sure I'm clear yet what the disruption is, given doctors usually only do a small number of tests at once. Certainly we should take less blood from patients generally but we do already for kids so could/should do it for everyone with existing technology," said Euan Ashley, an associate professor of cardiovascular medicine at Stanford University, in an email to WIRED. Theranos is already making this vision a reality. Their partnership with Walgreens will bring the new testing service to stores nationwide.

Regardless of whether Holmes' vision works out, there is one area where the company is already making a bold statement: It's listing how much each of its roughly 1,000 laboratory test costs. In May, the Center for Medicare & Medicaid Services released data on pricing for the 100 most commonly billed hospital discharges, highlighting huge variations even within cities. Data on diagnostic testing isn't yet readily available. At Theranos, the price is the same for everyone. The idea behind that level of transparency - which is not standard in the healthcare system - is to increase access and improve consumers' experience.

Today Holmes introduced the company's new mobile phone app, which will let patients check in to and make appointments from home. When they email a photo of their insurance card and lab order form, Theranos will inform them within minutes whether their tests are covered by their insurance and whether there is a co-pay. It's all in the name of fostering a system that allows patients to own and control their data, Holmes says. She argues that when people are buying something, they have the right to know what it's going to cost.

"It's a basic human right to be able to get tested," said Holmes. "Whether you're insured or uninsured, the price should be the same."

<http://www.livescience.com/41008-yasser-arafat-assassination-polonium.html>

### **Yasser Arafat's Death Linked to Radioactive Polonium**

*Since Yasser Arafat died in Percy Hospital in Paris of uncertain causes in 2004, rumors have swirled that the Palestinian leader may have been assassinated.*

By Marc Lallanilla, Assistant Editor | November 06, 2013 04:15pm ET

A new medical report lends considerable credibility to those claims: Investigators determined that Arafat's personal effects and his body, which was exhumed in 2012 for examination, contained extraordinary amounts of radioactive polonium-210, a lethal poison. In the carefully worded report, scientists from the University Centre of Legal Medicine in Lausanne, Switzerland, concluded that despite the years since Arafat's death and the quality of the specimens examined, "the results moderately support the proposition that the death was the consequence of poisoning with polonium-210."

This latest report about polonium in Arafat's remains confirms the results found by scientists earlier this year. An article published in the medical journal *The Lancet* in October reported that significant amounts of polonium were found on Arafat's toothbrush, underwear and other personal items.



**Proof of assassination?**

A growing number of experts believe this is incontrovertible proof that Arafat was assassinated.

"Yasser Arafat died of polonium poisoning," Dave Barclay, a British forensic scientist, told Al Jazeera. "The level of polonium in Yasser Arafat's rib ... is about 900 millibecquerels [unit of radioactivity]. That is either 18 or 36 times the average, depending on the literature."

Polonium is a soft, silvery-gray metal that was discovered by Pierre and Marie Curie in 1898; Marie named the element after her beloved native Poland. It has some industrial applications, such as eliminating static electricity in machine processes and as a heat source in satellites.

**Polonium's dark history**

Arafat isn't the only international figure believed to have been assassinated with polonium: Alexander Litvinenko, a Russian political dissident, was living in London in 2006 when he suddenly fell ill. Tests eventually revealed that polonium was not only in Litvinenko's body, but was also found throughout the restaurant where he had dined the day he first developed symptoms of radiation poisoning.

Though the evidence that Arafat was killed by polonium continues to mount, it's not clear who might have killed him. Leading suspects include political rivals within the Palestinian community or Israeli authorities, a claim that Israel has repeatedly denied - no evidence has emerged that links Israel to Arafat's death.

Suha Arafat, widow of the Palestinian leader, received a copy of the Swiss medical report on Tuesday (Nov. 5). "When they came with the results, I'm mourning Yasser again," she told Al Jazeera. "It's like you just told me he died." Additional reports are expected soon from French and Russian scientific teams, who were also given specimens of Arafat's personal items and bodily tissues to examine.

<http://www.livescience.com/41010-japan-tsunami-floating-debris.html>

**Tsunami Debris 'Island' Headed for US? NOAA Sets Record Straight**

*Debris from the deadly tsunami that struck Japan in 2011 is drifting across the Pacific Ocean toward North America, and will likely continue to wash onto North American shores over the next few years, according to the U.S. National Oceanic and Atmospheric Administration (NOAA).*

By Denise Chow, Staff Writer | November 06, 2013 04:50pm ET

"A significant amount of debris has already arrived on U.S. and Canadian shores, and it will likely continue arriving in the same scattered way over the next several years," NOAA officials said in a statement. "As we get further into the fall and winter storm season, NOAA and partners are expecting to see more debris coming ashore in North America, including tsunami debris mixed in with the 'normal' marine debris that we see every year."

On March 11, 2011, a 9.0-magnitude earthquake struck off the east coast of Japan, triggering a devastating tsunami that killed more than 15,000 people and caused widespread destruction. An estimated 5 million tons of debris - everything from boats to kitchen appliances - was swept into the Pacific Ocean by the tsunami.

Roughly 70 percent of this detritus likely sank near the coast of Japan, but the rest (some 1.5 million tons) is scattered in the water, and has been drifting toward North America. [Tracking Tsunami Debris (Infographic)] Recent reports suggested an island of debris the size of Texas was floating toward North America, but NOAA officials were quick to set the record straight. "At this point, nearly three years after the earthquake and tsunami struck Japan, whatever debris remains floating is very spread out," NOAA officials said. "It is spread out so much that you could fly a plane over the Pacific Ocean and not see any debris, since it is spread over a huge area, and most of the debris is small, hard-to-see objects."

NOAA has been tracking the debris since 2011, and the agency recently updated its models to include the effects of wind on the debris, which vary depending on the material and how much of the object's surface is above water. But there are still many unknowns surrounding where all that stuff will end up, and when pieces of debris may arrive on American shores.

"This new modeling effort gives us a better understanding of where the debris may have traveled to date, but it does not predict where it will go in the future or how fast it will drift," NOAA officials wrote in an update. "The new model takes into account that wind may move items at different speeds based on how high or low materials sit in the water."

Earlier this year, a small Japanese skiff washed ashore near Crescent City, Calif. Nearly 30 other pieces of debris - including fishing buoys, a soccer ball, other small boats and even two floating docks - have washed up in Oregon, Washington, Hawaii, Alaska and British Columbia.

The docks that were swept ashore in Washington and Oregon contained massive amounts of marine life, which required decontamination in order to prevent non-native invasive species from gaining a foothold along the U.S. coast.

<http://www.sciencedaily.com/releases/2013/11/131106202245.htm>

## **Clear Association Between ACE Inhibitors, Acute Kidney Injury**

*Cambridge scientists have found an association between ACE inhibitors (and similar drugs) and acute kidney injury -- a sudden deterioration in kidney function.*

ACE inhibitors and related drugs known as angiotensin receptor antagonists (ARAs or 'sartans') are the second most frequently prescribed medicines in UK clinical practice, and are used to treat common conditions such as high blood pressure, heart disease and kidney problems, especially in people with diabetes. Although concerns about a link between these drugs and kidney function have been raised in the past, the size of the problem had previously been unknown. The research is published today, 06 November, in the journal PLOS ONE.

The researchers therefore examined the issue using data from the whole of England. They compared the admission rates for acute kidney injury to English hospitals with the prescribing rates of ACE inhibitors and ARAs. From 2007/8 to 2010/11, there was a 52 per cent increase in acute kidney injury admissions. During this same period of time, there was an increase in the number of prescriptions for ACE inhibitors and ARAs issued by GP surgeries by 16 per cent.

The results show a clear association between the increase in prescriptions and the increase in hospital admissions. The researchers estimate that 1636 hospital admissions with acute kidney injury -- which has a mortality rate in the UK of around 25-30 per cent of patients -- could potentially have been avoided if the prescribing rate had remained at the 2007/8 levels. They estimate that one in seven cases of acute kidney injury could be due to increased prescriptions for these drugs.

This is the first time that a study has been able to assess the extent to which these medications are linked to acute kidney injury. However, the researchers emphasise that we cannot assume that the medication was a direct cause of the acute kidney injury in this study, and no one should stop taking these medications unless advised by their doctor to do so.

Dr Rupert Payne, senior author of the study from the University of Cambridge's Institute of Public Health, said: "There has been lots of anecdotal evidence suggesting these drugs may be a contributory factor in patients developing acute kidney injury, and this work gives us an opportunity to estimate the size of the problem, as well as making clinicians and patients more aware of the importance of using these drugs in accordance with current clinical guidelines." "As both a GP and clinical pharmacologist, it also highlights to me the importance of improving our understanding of the risks and benefits of drugs more generally in the real world of clinical practice, away from the artificial setting of clinical trials."

Dr Laurie Tomlinson, co-author of the study, added: "As a kidney doctor I have looked after many patients with acute kidney injury who were taking these medications prior to becoming unwell and have often worried that the drugs were doing more harm than good. These results are the first to estimate to what extent these drugs may be contributing to the growing incidence of acute kidney injury. Therefore, they represent the first step of research needed to better define when they can be prescribed safely, which should reduce the growing burden of acute kidney injury and save NHS costs and ultimately lives."

The researchers will next use large primary care databases to examine the association between the drugs and acute kidney injury for individual patients and, in particular, the role of other medication, patient factors (such as the existence of chronic kidney disease) and infections in causing acute kidney injury.

Laurie A. Tomlinson, Gary A. Abel, Afzal N. Chaudhry, Charles R. Tomson, Ian B. Wilkinson, Martin O. Roland, Rupert A. Payne. *ACE Inhibitor and Angiotensin Receptor-II Antagonist Prescribing and Hospital Admissions with Acute Kidney Injury: A Longitudinal Ecological Study*. PLoS ONE, 2013; 8 (11): e78465 DOI: 10.1371/journal.pone.0078465

[http://www.eurekalert.org/pub\\_releases/2013-11/hfhs-oci110713.php](http://www.eurekalert.org/pub_releases/2013-11/hfhs-oci110713.php)

## **Online course improves physicians skill level for detecting skin cancer**

*Primary care physicians who took an online training course about skin cancer detection significantly improved their skill to properly diagnose and manage benign and malignant lesions, according to a national study from Henry Ford Hospital in Detroit.*

DETROIT – The physicians' enhanced skill level also led to a reduction in unnecessary referrals to dermatology specialists. The INFORMED study is believed to be the first of its kind to track physician practice patterns as an outcome of a skin cancer detection training course. INFORMED stands for INternet curriculum FOR Melanoma Early Detection. Key findings of 54 physicians who took the course:

*Scores for diagnosing and managing all skin cancer lesions increased 10 percent.*

*Scores for diagnosing benign lesions increased 14 percent.*

*Patient referrals for suspicious lesions or new visits to a dermatology specialist declined as the result of improved detection by primary care physicians.*

*Physicians still retained their improved skill level six months later.*

The findings are published online in the November/December issue of the Journal of the American Board of Family Medicine at <http://www.jabfm.org/content/26/6/648.full>

"We all know the demands on a physician's time. But this online course shows that we can empower primary care physicians to know when they themselves can take care of some of these patients and have the confidence in doing so, and not drive up the cost of utilization with unnecessary referrals to a dermatologist," says Melody Eide, M.D., a Henry Ford dermatologist and the study's lead author.

Each year, there are more new cases of skin cancer than the combined incidence of breast, prostate, lung and colon cancers, according to the Skin Cancer Foundation. Treatment of nonmelanoma skin cancers has increased by nearly 77 percent between 1992 and 2006. Meanwhile, incidence rates of melanoma – the most serious form of skin cancer – have been increasing for at least 30 years. It is estimated that one in 50 Americans will develop melanoma by 2015.

Given these disconcerting trends, researchers sought to evaluate whether primary care physicians (PCP) could diagnose skin cancer if provided targeted, specific education. PCPs, after all, see more patients than any other physician group. Fewer than 30 percent of primary care residents receive training for performing a skin examination during their medical training.

"Improving PCPs skills at diagnosing and managing skin lesions is an important way to improve patient care because patients frequently bring skin complaints to their family doctor," Dr. Eide says.

The web-based course [http://www.skinsight.com/info/for\\_professionals/skin-cancer-detection-informed/skin-cancer-education](http://www.skinsight.com/info/for_professionals/skin-cancer-detection-informed/skin-cancer-education) covered the three most common skin cancers – basal cell carcinoma, squamous cell carcinoma and melanoma, and featured 450 clinical images of lesions. The participants chose from two web options - traditional textbook format and case-based format, which took about two to three hours to complete. The case-based format featured nine case studies with interactive self-assessment tests and immediate feedback.

Before taking the course in 2011, participants took a pretest of 25 images of skin lesions in which they had to choose a diagnosis and course of action – reassure or refer. Participants were assessed a post-test immediately after completing the course, then repeated six months later.

"Their post-test scores were much higher than their pre-test scores," Dr. Eide says. "The scores suggest that prior to taking the course, the participants had the most difficulty distinguishing between benign and malignant skin lesions. But taking the course improved their ability to do so."

*The INFORMED study involved nine U.S. health care institutions: Henry Ford Hospital, Kaiser Permanente, Harvard Medical School, Harvard Pilgrim Health Care Institute, Harvard School of Public Health, Memorial Sloan-Kettering Cancer Center, Veterans Affairs Medical Center, Rhode Island Hospital and Brown University.*

*The study was funded by the Melanoma Research Alliance.*

[http://www.eurekalert.org/pub\\_releases/2013-11/uog-rst110713.php](http://www.eurekalert.org/pub_releases/2013-11/uog-rst110713.php)

### **Research shows that the more chocolate you eat, the lower your body fat level is**

*University of Granada researchers from the Faculty of Medicine and the Faculty of Physical Activity and Sports Sciences have scientifically disproven the old belief that eating chocolate is fattening.*

In an article published this week in the journal Nutrition, the authors have shown that higher consumption of chocolate is associated with lower levels of total fat (fat deposited all over the body) and central fat (abdominal), independently of whether or not the individual participates in regular physical activity and of diet, among other factors.

The researchers determined whether greater chocolate consumption associated with higher body mass index and other indicators of total and central body fat in adolescents participating in the HELENA (Healthy Lifestyle in Europe by Nutrition in Adolescence) study. This project, financed by the European Union, studies eating habits and lifestyle in young people in 9 European countries, including Spain.

#### **Independent of diet and physical activity**

The study involved 1458 adolescents aged between 12 and 17 years and results showed that a higher level of chocolate consumption associated with lower levels of total and central fat when these were estimated through body mass index, body fat percentage - measured by both skinfolds and bioelectrical impedance analysis - and waist circumference. These results were independent of the participant's sex, age, sexual maturation, total energy intake, intake of saturated fats, fruit and vegetables, consumption of tea and coffee, and physical activity. As the principle author Magdalena Cuenca-García explains, although chocolate is considered a high energy content food - it is rich in sugars and saturated fats - "recent studies in adults suggest chocolate consumption is associated with a lower risk of cardiometabolic disorders".

In fact, chocolate is rich in flavonoids - especially catechins - which have many healthy properties: "they have important antioxidant, antithrombotic, anti-inflammatory and antihypertensive effects and can help prevent ischemic heart disease".

Recently, another cross-sectional study in adults conducted by University of California researchers found that more frequent chocolate consumption also associated with a lower body mass index. What's more, these results were confirmed in a longitudinal study in women who followed a catechin-rich diet.

The effect could be partly due to the influence of catechins on cortisol production and on insulin sensitivity, both of which are related with overweight and obesity.

### **Calorie impact is not the only thing that matters**

The University of Granada researchers have sought to go further and analyse the effect of chocolate consumption at a critical age like adolescence by also controlling other factors that could influence the accumulation of fat. The research, which is both novel and, perhaps, the largest and best-controlled study to date, is the first to focus on the adolescent population. It includes a large number of body measures, objective measurement of physical activity, detailed dietary recall with 2 non-consecutive 24-hour registers using image-based software, and controls for the possible effect of a group of key variables.

In Nutrition, the authors stress that the biological impact of foods should not be evaluated solely in terms of calories. "The most recent epidemiologic research focuses on studying the relation between specific foods - both for their calorie content and for their components - and the risk factors for developing chronic illnesses, including overweight and obesity".

Despite their results, the authors insist that chocolate consumption should always be moderate. "In moderate quantities, chocolate can be good for you, as our study has shown. But, undoubtedly, excessive consumption is prejudicial. As they say: you can have too much of a good thing".

*The University of Granada researchers stress that their findings "are also important from a clinical perspective since they contribute to our understanding of the factors underlying the control and maintenance of optimal weight".*

*Association between chocolate consumption and fatness in European adolescents Magdalena Cuenca-García, Jonatan R. Ruiz, Francisco B. Ortega, Manuel J. Castillo Nutrition (2013). <http://dx.doi.org/10.1016/j.nut.2013.07.011>*

[http://www.eurekalert.org/pub\\_releases/2013-11/cp-ssi103113.php](http://www.eurekalert.org/pub_releases/2013-11/cp-ssi103113.php)

### **Social symptoms in autistic children may be caused by hyper-connected neurons**

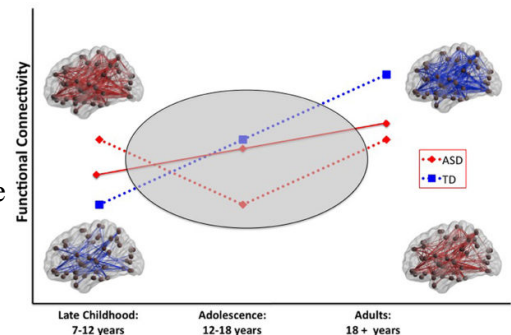
***The brains of children with autism show more connections than the brains of typically developing children do.***

What's more, the brains of individuals with the most severe social symptoms are also the most hyper-connected. The findings reported in two independent studies published in the Cell Press journal Cell Reports on November 7th are challenge the prevailing notion in the field that autistic brains are lacking in neural connections.

The findings could lead to new treatment strategies and new ways to detect autism early, the researchers say.

Autism spectrum disorder is a neurodevelopmental condition affecting nearly 1 in 88 children.

"Our study addresses one of the hottest open questions in autism research," said Kaustubh Supekar of Stanford University School of Medicine of his and his colleague Vinod Menon's study aimed at characterizing whole-brain connectivity in children. "Using one of the largest and most heterogeneous pediatric functional neuroimaging datasets to date, we demonstrate that the brains of children with autism are hyper-connected in ways that are related to the severity of social impairment exhibited by these children."



***The brains of children with autism show more connections than the brains of typically developing children do. What's more, the brains of individuals with the most severe social symptoms are also the most hyper-connected. The findings reported in two independent studies published in the Cell Press journal Cell Reports on Nov. 7 are challenge the prevailing notion in the field that autistic brains are lacking in neural connections.*** Cell Reports, Keown et al

In the second Cell Reports study, Ralph-Axel Müller and colleagues at San Diego State University focused specifically on neighboring brain regions to find an atypical increase in connections in adolescents with a diagnosis of autism spectrum disorder. That over-connection, which his team observed particularly in the regions of the brain that control vision, was also linked to symptom severity.

"Our findings support the special status of the visual system in children with heavier symptom load," Müller said, noting that all of the participants in his study were considered "high-functioning" with IQs above 70. He says measures of local connectivity in the cortex might be used as an aid to diagnosis, which today is based purely on behavioral criteria.

For Supekar and Menon, these new views of the autistic brain raise the intriguing possibility that epilepsy drugs might be used to treat autism. "Our findings suggest that the imbalance of excitation and inhibition in the local brain circuits could engender cognitive and behavioral deficits observed in autism," Menon said.



That imbalance is a hallmark of epilepsy as well, which might explain why children with autism so often suffer with epilepsy too. "Drawing from these observations, it might not be too farfetched to speculate that the existing drugs used to treat epilepsy may be potentially useful in treating autism," Supekar said.

*Cell Reports, Keown et al.: "Local functional overconnectivity in posterior brain regions is associated with symptom severity in autism spectrum disorders."*

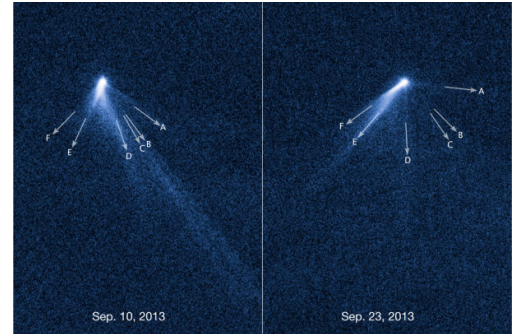
[http://www.eurekalert.org/pub\\_releases/2013-11/uoc--ad110613.php](http://www.eurekalert.org/pub_releases/2013-11/uoc--ad110613.php)

## 'Freakish' asteroid discovered, resembles rotating lawn sprinkler

*Astronomers have discovered a "weird and freakish object" resembling a rotating lawn sprinkler in the asteroid belt between Mars and Jupiter.*

The find, reported online in the Nov. 7 issue of the *Astrophysical Journal Letters*, has left them scratching their heads and searching for an explanation for the strange asteroid's out-of-this-world appearance. Normal asteroids appear simply as tiny points of light. This bizarre asteroid has six comet-like tails of dust radiating from it like spokes on a wheel.

"It's hard to believe we're looking at an asteroid," said lead investigator David Jewitt, a professor in the UCLA Department of Earth and Space Sciences and the UCLA Department of Physics and Astronomy. "We were dumbfounded when we saw it. Amazingly, its tail structures change dramatically in just 13 days as it belches out dust."



**Labelled view of extraordinary multi-tailed asteroid P/2013 P5** NASA, ESA, D. Jewitt (University of California, Los Angeles), J. Agarwal (Max Planck Institute for Solar System Research), H. Weaver (Johns Hopkins University Applied Physics Laboratory), M. Mutchler (STScI), and S. Larson (University of Arizona)

One interpretation is that the asteroid's rotation rate increased to the point where its surface started flying apart, ejecting dust in episodic eruptions, starting last spring. The team has ruled out a recent asteroid impact scenario because a large quantity of dust would have been blasted into space all at once. This object, designated P/2013 P5, has ejected dust for at least five months, Jewitt said.

The asteroid was first seen as an unusually fuzzy-looking object with the Pan-STARRS survey telescope in Hawaii. Its multiple tails were discovered in images taken by NASA's Hubble Space Telescope on Sept. 10, 2013. When Hubble returned to the asteroid on Sept. 23, its appearance had totally changed; it looked as if the entire structure had swung around. "We were completely knocked out," said Jewitt.

The tails could have been formed by a series of "impulsive dust-ejection events," modeling by team member Jessica Agarwal revealed. Agarwal, of the Max Planck Institute for Solar System Research in Lindau, Germany, calculated that the first ejection event occurred on April 15 and the last one on Sept. 4. The intervening eruptions occurred on July 18, July 24, Aug. 8 and Aug. 26.

Radiation pressure from the sun smears out the dust into streamers. The asteroid could possibly have been spun up if the pressure of sunlight exerted a torque on the body, Jewitt said.

If its spin rate became fast enough, he said, the asteroid's weak gravity would no longer be able to hold it together. Dust might avalanche downslope toward the asteroid's equator and eventually drift into space to make a tail. So far, only a small fraction of the asteroid's main mass - perhaps 100 to 1,000 tons of dust - has been lost, Jewitt said. The 700-foot-radius nucleus is thousands of times more massive. Follow-up observations may reveal whether the dust leaves the asteroid in the equatorial plane; if so, that would indicate a "rotational breakup," Jewitt said.

This must be a common phenomenon in the asteroid belt, Jewitt said, and may even be the main way in which small asteroids die. "In astronomy, where you find one, you eventually find a whole bunch more," he said.

"This is an amazing object and almost certainly the first of many more to come."

The object may be a piece from an asteroid collision that occurred roughly 200 million years ago, Jewitt noted. The resulting collision fragments, known as the Flora asteroid family, are still following similar orbits.

Meteorites from these bodies show evidence of having been heated to as much as 1,500 degrees Fahrenheit.

*Jewitt, who is a faculty member in the UCLA College of Letters and Science is a member of the National Academy of Sciences and a fellow of both the American Association for the Advancement of Science and the American Academy of Arts and Sciences. He played an instrumental role in the 1993 discovery of the Kuiper Belt beyond Neptune. The discovery of the Kuiper Belt, which contains more than a billion objects and was once believed to be empty space, has fundamentally changed the modern perception of the solar system.*

*Co-authors of the current research are Jessica Agarwal (Max Planck Institute), Harold Weaver (Johns Hopkins Applied Physics Laboratory), Max Mutchler (Space Telescope Science Institute) and Stephen Larson (University of Arizona).*

*The research is funded by NASA. For images and more information about P/2013 P5, visit <http://hubblesite.org/news/2013/5>.*

[http://www.eurekalert.org/pub\\_releases/2013-11/ehs-pdf110713.php](http://www.eurekalert.org/pub_releases/2013-11/ehs-pdf110713.php)

## **Peptide derived from cow's milk kills human stomach cancer cells in culture**

*Findings reported in the Journal of Dairy Science show promise for treatment of gastric cancer*

Philadelphia, PA, – New research from a team of researchers in Taiwan indicates that a peptide fragment derived from cow's milk, known as lactoferricin B25 (LFcinB25), exhibited potent anticancer capability against human stomach cancer cell cultures. The findings, published in the Journal of Dairy Science®, provide support for future use of LFcinB25 as a potential therapeutic agent for gastric cancer.

"Gastric cancer is one of the most common causes of cancer-related mortality worldwide, especially in Asian countries," says Wei-Jung Chen, PhD, of the Department of Biotechnology and Animal Science of National Ilan University, Taiwan Republic of China. "In general, the main curative therapies for gastric cancer are surgery and chemotherapy, which are generally only successful if the cancer is diagnosed at an early stage. Novel treatment strategies to improve prognosis are urgently needed."

Investigators evaluated the effects of three peptide fragments derived from lactoferricin B, a peptide in milk that has antimicrobial properties. Only one of the fragments, LFcinB25 reduced the survival of human AGS (Gastric Adenocarcinoma) cells in a dose-dependent and time-dependent manner.

Under a microscope the investigators could see that after an hour of exposure to the gastric cancer cells, LFcinB25 migrated to the cell membrane of the AGS cells, and within 24 hours the cancer cells had shrunken in size and lost their ability to adhere to surfaces. In the early stages of exposure, LFcinB25 reduced cell viability through both apoptosis (programmed cell death) and autophagy (degradation and recycling of obsolete or damaged cell parts). At later stages, apoptosis appeared to dominate, possibly through caspase-dependent mechanisms, and autophagy waned.

"This is the first report describing interplay between apoptosis and autophagy in LFcinB-induced cell death of cancer cells," says Dr. Chen.

The research also suggested a target, Beclin-1, which may enhance LFcinB25's cytotoxic action. Beclin-1 is a protein in humans that plays a central role in autophagy, tumor growth, and degeneration of neurons. In this study, the investigators found that cleaved beclin-1 increased in a time-dependent manner after LFcinB25-exposure, suggesting to the authors a new approach in drug development that may boost the anticancer effects of LFcinB25.

"Optimization of LFcinB using various strategies to enhance further selectivity is expected to yield novel anticancer drugs with chemotherapeutic potential for the treatment of gastric cancer," concludes Dr. Chen.

<http://bit.ly/1hXAICf>

## **Africa's war on cancer kicks off with vaccine trials**

*This week sees the start of a programme trialling the introduction of the cervical cancer vaccine in Ghana*

15:00 07 November 2013 by Linda Geddes

AT FIRST, Florence Agyei put the bleeding down to the birth of her daughter 18 months earlier. "I thought maybe something had been left inside me," she says. She didn't think it was a disease and had never even heard the words kokoram awotea amo – cancer of the neck of the womb.

After enduring the pain and bleeding for seven months, it was a radio programme that finally prompted Florence, a Ghanaian market stall vendor, to seek help. At 36, she was diagnosed with advanced cervical cancer. Cancer is often seen as a disease of the affluent, hitting people in their twilight years.

Yet more than half of cancers now affect people in developing countries – often in the prime of their life. Africa recorded 681,000 new cancer cases in 2008 and that is predicted to double by 2030 – even before increased tobacco use and lifestyle changes are taken into account. Similar rises are expected in Latin America and some countries in Asia – attention was drawn to China this week when it was claimed the nation's youngest lung cancer patient is just 8 years old – but Africa is the least well equipped to deal with the increase. The good news is that there are vaccines that could prevent many cancer deaths – if the infrastructure and the political will are there to deliver them.

This week sees the start of a programme trialling the introduction of the cervical cancer vaccine in Ghana, and Niger and Madagascar will begin similar programmes later this month. The vaccines are supplied by the GAVI Alliance, but countries will have to demonstrate that they can deliver them in limited areas before vaccination is rolled out more widely. Rwanda is expected to be the first African country to start offering vaccination to all teenage girls early next year.

Infectious agents account for just 3 to 4 per cent of cancers in Western countries, but in Africa they're responsible for one-third, mostly because screening programmes aren't in place to catch the precancerous signs.

Cervical and liver cancer, which can be caused by the human papillomavirus (HPV) and hepatitis B virus respectively, each account for about 10 per cent of cancer deaths – and vaccines exist for both. It is hoped that combining vaccination with other preventative measures like screening, and encouraging people to eat well and give up smoking, could make a serious dent in Africa's cancer death toll.

"There's a big opportunity to avoid some of the mistakes of Western countries," says Christopher Wild, director of the World Health Organization's International Agency for Research on Cancer. "We're trying to convince people that they need to act now to prevent the problems of tomorrow."

That's difficult though, because many African governments already have their hands full reducing deaths related to childbirth and fighting diseases like HIV and malaria. They don't necessarily want to hear about something that is going to cause problems in a decade or so.

Yet breast and cervical cancer have already overtaken childbirth-related deaths in Asia and Latin America, and by 2030, African deaths from non-communicable diseases including cancer and heart disease are expected to eclipse the combined toll from infectious disease, malnutrition and death during childbirth.

"We're not suggesting that we need to take resources away from other areas like HIV, but we need to start re-evaluating our allocation of resources," says Vivien Davis Tsu of PATH, a non-profit organisation in Seattle. One possibility is piggybacking existing health infrastructures that have been set up to tackle HIV, using it to offer cancer screening at the same time as people come to collect antiretroviral medication, for example (see "Vinegar: The acid test for cancer"). Access to drugs and radiotherapy to treat advanced cancers is also a necessity, but remains largely unaffordable for many countries.

There are already signs that vaccination may work. Rwanda was the first African country to pilot HPV vaccination in 2011 and, unlike the vaccine's lukewarm reception in the US, where uptake has stagnated at around 50 per cent, Rwanda achieved 93 per cent coverage (Bulletin of the WHO, doi.org/pvf).

"Because we have a country where vaccination for other diseases has really paid off and people are seeing their children live, we have created trust," says Agnes Binagwaho, Rwanda's health minister. "In America, there are so many treatments. They don't understand that prevention is less expensive."

Hepatitis B vaccination is also now being offered to infants in most African countries, and vaccines against *Helicobacter pylori* – a bacterium that causes stomach cancer – and a more effective vaccine for HPV are in development.

Although vaccination won't prevent other burgeoning cancers like breast cancer, the hope is it will at least facilitate discussion about them. "HPV vaccination is the first concerted effort to address a cancer in developing countries," says Tsu. "This could be the thing that opens the doors to other cancer efforts."

Although Florence hadn't heard of the HPV vaccine, she says she would encourage her daughters, both under 12, to have it in the future. "If the vaccine is coming to protect girls, I think most women would want their daughters to be vaccinated."

For now, the radiotherapy – and the chemotherapy she has been paying for out of her wages – seem to be working. The bleeding has stopped and she is in less pain than before. More than anything, she wants to survive to see her children grow up. "When I first found out I had cancer I told my husband and son, and we all cried," she says, because death seemed inescapable. "Now I hope I can be cured."

### **Vinegar: The acid test for cancer**

How do you tackle cancer when your country has a tiny health budget and one oncologist for 16 million people?

When gynaecologist Mary Sue Makin worked at the Mulanje Mission hospital in Malawi in the early 2000s, she saw a new cervical cancer case every week. By the time the women arrived it was often too late. The country has no chemotherapy drugs, no radiation and for advanced cervical cancer, surgery doesn't usually help. All Makin had to offer was pain relief – morphine from the AIDS clinic next to her office.

That sparked an idea: plenty of women were visiting the clinic to pick up antiretroviral drugs, so Makin started offering cervical cancer screening at the same time. Women with HIV are at particularly high risk of developing cervical cancer.

Effective screening can be done for just \$2 per person, using acetic acid – vinegar – which turns precancerous cells white. Any seen can be frozen off using carbon dioxide before they become tumours.

Makin began offering the service at Mulanje Hospital in 2001, and soon started visiting the hospital's family planning clinic too. The idea was to try to catch women as early as possible, while surgery was a still an option. "It is a very positive way to reach people at high risk," she says.

<http://phys.org/news/2013-11-nanoparticles-drug-resistance-breast-cancer.html>

## **Nanoparticles can overcome drug resistance in breast cancer cells**

*Nanoparticles filled with chemotherapeutic drugs can kill drug-resistant breast cancer cells, according to a study published in the scientific journal Biomaterials.*

Nanoparticles are just as small, or even smaller, than many blood proteins. They can therefore pass through the walls of healthy and sick cells, which make them interesting carriers of drugs against cancer and other diseases. In the present study, researchers from Karolinska Institutet have shown that nanoparticles made from biodegradable plastics can overcome drug resistance in breast cancer cells. Such resistance is especially common in relapsing cancer patients and depresses, even neutralises the effect of the therapy against the tumour in many instances.

In their experiments, the researchers used breast cancer cells that responded poorly to drugs owing to their high concentrations of the enzyme microsomal glutathione S-transferase-1 (MGST-1). Abnormally high levels of MGST-1 have been associated with poor responses to several cancer drugs. The team treated the resistant breast cancer cells with nanoparticles filled with doxorubicin, a chemotherapeutic used clinically to treat bladder, lung, ovarian and breast cancer, amongst others.

"Our experiments on cultivated cells showed that the particles themselves are harmless," says research team member Dr Andreas Nyström, Associate Professor at the Institute of Environmental Medicine, Karolinska Institutet. "We made it possible for the nanoparticles carrying the drug to kill resistant cancer cells by controlling where in the cancer cell they delivered their payload. This improved the efficacy of the drug even at a much lower dose, which is important for limiting the adverse reactions to therapy."

Nanoparticles can also be used to control where the drug is delivered in the body, and the team is now planning to equip them with targeting groups such as peptides or antibodies, that direct them to specific tumour cells to increase the uptake of the particles and their drug content by the tumour while sparing healthy cells.

*More information: 'Nanoparticle-Directed Sub-cellular Localization of Doxorubicin and the Sensitization Breast Cancer Cells by Circumventing GST-Mediated Drug Resistance', Xianghui Zeng, Ralf Morgenstern, Andreas M. Nyström, Biomaterials, corrected proof online 6 November 2013. [www.sciencedirect.com/science/article/pii/S0142961213012726](http://www.sciencedirect.com/science/article/pii/S0142961213012726)*

<http://nyti.ms/1c220fi>

## **High Above Sea Level, Evolutionary Hot Spots**

*Páramos blanketing the Andes between 9,200 and 14,800 feet are like islands in a sea of forest*

By CARL ZIMMER

In 1799 the great naturalist Alexander von Humboldt and his companions set out from Caracas, Venezuela, to climb the Andes. They struggled up a mountainside, enveloped in mist so thick they had to clamber over rocks by hand. When the fog cleared, von Humboldt was left astonished by the view. Vast grasslands stretched all around him, home to an astonishing number of different trees, shrubs, and flowers.

"Nowhere, perhaps, can be found collected together, in so small a space, productions so beautiful and so remarkable in regard to the geography of plants," von Humboldt later wrote.

Von Humboldt had stumbled into a remarkable ecosystem, known as a Páramo. Páramos blanket the Andes in Venezuela, Ecuador and Colombia, growing at altitudes between 9,200 and 14,800 feet above sea level.

"They're like islands in a sea of forest," said Santiago Madriñán, an expert on Páramos at the University of the Andes in Colombia. All told, Páramos cover about 13,500 square miles - an area the size of Maryland. In that small space, Dr. Madriñán and other researchers have found 3,431 species of vascular plants, most of them found nowhere else on Earth. The Páramos are home to strange variations on familiar forms, such as a daisy known as *Espeletia uribei* that grows as tall as trees. But according to a new study, the Páramos are even more remarkable than von Humboldt could have realized. They are the fastest evolving place on Earth.

Scientists have long known that in certain spots, evolution runs faster than normal. The Galápagos Islands, for example, are home to some 13 species of Darwin's finches, which all evolved from a single group of birds that originally colonized them. The archipelago is just a few million years old, however, which means that all their diversity has evolved in a geologically short period of time.

In recent years, scientists have identified other regions where evolution is running fast. To measure its speed, researchers have looked at the DNA of species living in each place. The longer it has been since two species diverged from a common ancestor, the more time each lineage has had to accumulate mutations. Young species have relatively few mutations.

Dr. Madriñán has studied Páramos for over a decade, and he's long suspected that evolution is running fast in them as well. "I don't know if it was a hunch or what it was, but when you study the Páramos, it's a marvelous place," he said.



The geology also gave support to his hunch. The Andes started forming tens of millions of years ago, but it wasn't until 2.5 million years ago that the northern Andes rose above the elevation where trees can survive. Only then could all the diversity of the Páramos emerge.

To calculate the speed of evolution in the Páramos, Dr. Madriñán and his colleagues surveyed 13 different lineages of plants that grow there. They estimated the rate at which species had split from each other in each lineage, and then combined those estimates into a single average. The scientists then looked at data on plants that grow in other fast-evolving places, such as Hawaii and the Mediterranean coast.

The results surpassed Dr. Madriñán's suspicions. The Páramos wasn't just home to fast evolution, it turned out. Of the eight places he and his colleagues compared, the Páramos are evolving the fastest of all.

Other experts on evolutionary rates are intrigued by the new study, which was published last month in *Frontiers in Genetics*. "Of course these results are still very preliminary," said Luis Valente of the University of Potsdam, noting that scientists have only sampled a few groups of plants from each evolutionary hot spot. But Dr. Valente thought the study persuasively demonstrates that the Páramos is a special place. "This may be a region where evolution is proceeding at a very fast pace, and where many new species may still be in the process of being formed," he said.

Michael Sanderson of the University of Arizona thinks the contest won't be settled definitively until biologists can draw large-scale evolutionary trees. "Then we'll finally sort out the hottest hot spots," he said.

Dr. Madriñán suspects that the peculiar climate of the Páramos is responsible for their fast evolution. Because the grasslands are at the Equator, they are bathed in sunshine year-round. But to take advantage of that ample energy, the plants also have to contend with cold temperatures and harsh ultraviolet rays, not to mention weather that can turn on a dime. "You may be in total mist and then half an hour later you are in total sunshine," said Dr. Madriñán.

When plants began to spread into the newly formed Páramos, Dr. Madriñán suspects, they evolved many solutions to surviving there. They specialized on different niches, from damp bogs to dry hillsides and stands of shrubs and trees. Páramo plants also evolved a wide range of defenses against the elements. *Espeletia uribei*, the daisy tree, grows white hairs on its flowers to protect them from damaging ultraviolet rays, while covering its stem with a thick layer of dead leaves to keep it warm.

Dr. Madriñán and his colleagues are now exploring the history of the plants to see if they can explain their remarkable speed. "Páramos are the new laboratory to study evolution happening at incredible rates," he said.

<http://www.livescience.com/41028-lice-reveal-clues-to-human-evolution.html>

### **Lice Reveal Clues to Human Evolution**

*Clues to human evolution generally come from fossils left by ancestors and the molecular trail encoded in the human genome as it is tweaked over generations. However, some researchers are looking to another source: the bloodsucking louse.*

By Wynne Parry, LiveScience Contributor | November 07, 2013 12:55pm ET

GAINESVILLE, Fla. - Lice have been closely associated with humans for millennia; in spite of human attempts to get rid of the parasites, their persistence has made them a potential reservoir of information for those who want to know more about human evolution and history, said David Reed, associate curator of mammals at the Florida Museum of Natural History, on Sunday (Nov. 3) here at the ScienceWriters2013 conference.

"When we went through our evolutionary history, we didn't do it by ourselves - we took a whole bunch of passengers with us," Reed said. Clues from the bloodsucking hitchhikers, for instance, suggest modern humans intermingled with Neanderthals (a theory also supported by other genetic research) and that humans may have first put on clothing before leaving Africa.

#### **Parasitic passengers with a story**

Like family members on the same road trip, these passengers - otherwise known as parasites, including lice - can offer differing versions of the adventure, filling in gaps in other accounts, Reed said. He and colleagues have been looking to lice genomes to do just that. [The 10 Most Diabolical and Disgusting Parasites]

Lice, which infect many animals, are excellent trackers for their hosts' evolution. They spend their entire lives on their host, perish after a relatively short period of time if they fall off, and infest a single species of host, Reed told an audience at the conference sponsored by the National Association of Science Writers.

Humans are unusual among lice hosts; they provide homes for more than one species of lice. The pubic louse looks quite different from its counterparts in human hair and clothing. Through genetic analysis, Reed and colleagues determined that more than 3 million years ago, the human pubic louse originated from gorilla lice, where it adapted to grab onto large hairs spread farther apart. This finding means that humans and gorillas must have lived in close proximity during this time period. The information is significant, because gorilla fossils from this time are virtually nonexistent, Reed said.

Reed and colleagues have also looked at the split between head and clothing lice for clues as to when humans began wearing clothes. They found that clothing lice diverged from head lice between 80,000 and 170,000 years ago, most likely at the earlier end of that range. This means humans were likely tinkering with clothing use before leaving Africa, Reed said.

### **A record of long-gone ancestors?**

Lice genomes may also reveal information about interactions between modern humans' long-gone ancestors and relatives. Researchers have identified three major lineages, dubbed Clades A, B and C, within the DNA from the mitochondria, or energy-producing centers of cells, of lice collected in sites around the world. Using variations in the DNA to look back in time, the researchers saw these groups had a common ancestor about 2 million years ago. Clade C then split off from the group. Much later, between 700,000 and 1 million years ago, Clade B split from A.

The timing of these splits, and the modern geographic distribution of these clades have led the researchers to suggest that C evolved on *Homo erectus* as this hominid emerged, and that B evolved on Neanderthals. But these three louse lineages did not stay apart. Some interaction, such as hunting together, brought humans' ancient, lice-infested ancestors close enough to reunite the three lineages all of which are now carried by modern humans, Reed and others suggest.

They are continuing work to understand better the histories encoded in lice DNA. With the caveat that the following work has not yet been vetted by the peer-review process, Reed said computer simulations of lice genetic evolution support this story. Meanwhile, full genome sequences from lice in Clades A and B indicate the two are interbreeding. (C is much rarer, and the researchers' samples turned out to be too degraded to sequence.) Reed's lab is also applying lice genomics to study how people arrived in the Americas.

<http://www.sciencedaily.com/releases/2013/11/131107142438.htm>

## **Children Born Prematurely Face Up to 19 Times Greater Risk of Retinal Detachment**

*Children born extremely prematurely have up to a 19 times greater risk of retinal detachment later in life than peers born at term*

Children born extremely prematurely have up to a 19 times greater risk of retinal detachment later in life than peers born at term, according to a Swedish study published this month in *Ophthalmology*, the journal of the American Academy of Ophthalmology. In the first large population-based, long-term investigation of the association between preterm birth and later retinal detachment, the research determined that birth before 32 weeks is associated with increased risks of retinal detachment in childhood, adolescence and young adult life. The study's findings indicate the need for ophthalmologic follow-up in children and adults born extremely and very prematurely. The United States has the sixth largest number of premature births, with more than 500,000 premature babies born each year.

The researchers used Swedish nationwide population registries of more than three million births from 1973 to 2008 to identify subjects born prematurely (at less than 37 weeks of gestation), who were then separated into two groups: those born between 1973 and 1986, at which point a national retinopathy of prematurity (ROP) screening program was established, and those born between 1987 and 2008. ROP is a condition that causes abnormal blood vessels to grow in the retina (back of the eye) and can cause retinal detachment, which is a major cause of childhood blindness globally. A detached retina may lead to vision loss and even blindness unless it is treated with surgery. Although the connection between retinal detachment and preterm births has been noted in smaller studies, this is the first study to analyze a population of this size.

For those born extremely prematurely (less than 28 weeks of gestation) between 1973 and 1986, the researchers found the risk of retinal detachment was 19 times higher than peers born at term. Those born extremely prematurely between 1987 and 2008 had a nine-fold increase in risk after adjustment for potential cofounders. Those born very prematurely (28 to 31 weeks of gestation) between 1973 and 1986 had a four-fold increased risk and those born very prematurely between 1987 and 2008 had a three-fold greater risk than those born at term. Additionally, the researchers found that moderately preterm birth (32 to 36 weeks of gestation) was not associated with an increased risk of retinal detachment.

"We may just be seeing the tip of the iceberg of late ophthalmic complications after preterm birth," said Anna-Karin Edstedt Bonamy, M.D., Ph.D., pediatrician at Karolinska Institutet in Stockholm and the study's lead researcher. "Not only does the risk of retinal detachment increase with age, but there has also been an increase in survival among people born prematurely since the 1970s. This provides opportunities for future research to address if the increased risk persists among those born prematurely as they age."

Clinical studies and care series indicate that individuals born prematurely may be at lifelong risk for ophthalmologic complications other than ROP. This includes an increased risk of subnormal visual acuity,

visual perceptual problems, strabismus, refractive errors (particularly high myopia) and reduced contrast sensitivity and visual fields.

The American Academy of Pediatrics, along with the American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus and the American Association of Certified Orthoptists recommend screening for ROP in infants born at less than 30 weeks of gestation or those with a birth weight of less than 1500 grams (or those with a birth weight of less than 2000 grams with an unstable clinical course). Although follow-up guidelines vary from country to country, the researchers recommend that individuals who have been treated for ROP in the neonatal period should continue follow up on a yearly basis.

*Anna-Karin E. Bonamy, Gerd Holmström, Olof Stephansson, Jonas F. Ludvigsson, Sven Cnattingius. Preterm Birth and Later Retinal Detachment. Ophthalmology, 2013; 120 (11): 2278 DOI: 10.1016/j.ophtha.2013.03.035*

<http://www.livescience.com/41048-facts-about-homo-erectus.html>

## Homo Erectus: Facts About the 'Upright Man'

*Homo erectus, or "upright man," was an ancient ancestor of modern humans that lived between 2 million and 100,000 years ago.*

By Tia Ghose, Staff Writer | November 07, 2013 06:04pm ET

Compared to modern Homo sapiens, which evolved just 200,000 years ago, the ancient man had a long reign. H. erectus is the first human ancestor to have similar limb and torso proportions to those seen in modern humans, without the adaptations needed to swing from the branches, suggesting it had adapted to walking on two feet in a more open, grassland environment.

### Body size

Homo erectus was taller than earlier human ancestors. For instance, one of the most complete fossil skeletons ever found, a 1.5-million-year-old specimen of an adolescent male known as Turkana Boy, was 5 feet 3 inches (1.6 meters) tall. The iconic, 3.2-million-year-old Australopithecus skeleton dubbed Lucy, in comparison, was just 3 feet 7 inches (1.1 meters) tall at death. The species also had more variation in height - with more tall and short individuals - than more primitive humans.



*A reconstruction of a Homo erectus female (based on fossil ER 3733) by paleoartist John Gurche, part of the Smithsonian National Museum of Natural History's Human Origins Program.*

Notably, H. erectus also had much larger brains than its precursors. Those bigger brains and bodies required more food and energy to survive. Wear on the teeth of H. erectus fossils suggest the ancient man ate a fairly diverse diet, and most scientists believe the species ate more animal protein compared to older human species. Homo erectus' larger brain may explain why it displays so many distinctly human behaviors. For instance, ancient tools reveal the human ancestor was butchering animals by at least 1.75 million years ago, and may have harnessed fire to cook food as early as 1.9 million years ago. The species' increased smarts may have also enabled it to expand into so many different environments.

### Lineage

Homo erectus likely first evolved from an earlier human ancestor, known as Homo habilis, somewhere in East Africa, but spread out from there. Fossils dating from about 1.8 million years ago until about 100,000 years ago have been found in Southeast Asia, Europe, the Caucasus, India and China.

H. erectus would eventually give rise to a host of other early humans, such as Homo heidelbergensis and Homo floresiensis, though scientists still don't agree on whether the species is a direct human ancestor to Homo sapiens. Anthropologists also disagree on whether all the Homo erectus fossils found around the world represent one species, or several slightly different ones (some anthropologists consider Turkana Boy, for instance, to be a slightly different species dubbed Homo ergaster).

[http://www.eurekalert.org/pub\\_releases/2013-11/uos-ntf110813.php](http://www.eurekalert.org/pub_releases/2013-11/uos-ntf110813.php)

## New test for patients with sore throats cuts antibiotic use by nearly a third

*A new 'clinical score' test for patients with sore throats could reduce the amount of antibiotics prescribed and result in patients feeling better more quickly, research in the British Medical Journal shows.*

Researchers at the University of Southampton, funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme, used the five-item FeverPAIN score to decide whether to prescribe patients with an antibiotic immediately or to give them a delayed prescription and compared it with simply offering a delayed prescription.

The FeverPAIN score includes; fever in the past 24 hours, a pus infection, rapid attendance (within three days), inflamed tonsils and no cough or cold symptoms.



Results showed that using the test reduced antibiotic use by almost 30 per cent and despite using fewer antibiotics, patients in the FeverPAIN score group experienced a greater improvement in symptoms. But the use of an in-practice rapid antigen test (a test which detects the bacteria, Lancefield Group A Streptococcus, which is the most common bacterium to cause sore throats) in conjunction with the FeverPAIN score did not result in any further reductions in antibiotic use or improvements in symptoms.

Paul Little, Professor of Primary Care Research who led the research, comments: "Our findings show that using this clinical score test can target antibiotics more effectively and help persuade patients antibiotics are not needed." Additionally the FeverPAIN score should enable better targeting of antibiotics than the current scoring system to identify the likelihood of a bacterial infection in patients complaining of a sore throat, as it allows GPs to rule out likely streptococcal infection in more patients."

The study recruited 631 patients with an acute sore throat and compared use of the FeverPAIN clinical score, with or without rapid antigen testing, with a delayed prescription, in which patients were told to pick up a prescription three to five days later if their symptoms did not settle or got worse.

Patients who had four or five of the clinical features of the FeverPAIN test were prescribed antibiotics immediately; a delayed antibiotic prescription was offered to patients with two or three features and no antibiotics to those with only one or no features.

The test led to a 29 per cent reduction in antibiotic use compared with the delayed prescription approach. One in three patients in the FeverPAIN score group said their sore throat had improved rapidly from a moderately bad problem to a slight problem within two to four days. Moderately bad or worse symptoms also got better faster in the clinical score group.

However, the use of a rapid antigen test as well as the FeverPAIN test for patients who displayed streptococci symptoms did not offer any further improvements, with a 27 per cent reduction in antibiotic use as well as similar improvements in patients' symptoms.

Study co-author Dr Michael Moore, a GP and a reader in primary care research at the University of Southampton, adds: "Clinicians can consider using a clinical score to target antibiotic use for acute sore throat, which is likely to reduce antibiotic use and improve symptom control. There is no clear advantage in the additional use of a rapid antigen test.

"We found that the FeverPAIN score picks up bacterial throat infections more accurately than the current scoring system and importantly picks up larger numbers of patients who are at low risk of streptococcal infection giving the patient and the doctor the confidence not to use antibiotics. If you select those at the highest risk of streptococcal infection then antibiotics can be more targeted at the people who are most likely to get symptom benefit."

[http://www.eurekalert.org/pub\\_releases/2013-11/uoha-hpp110813.php](http://www.eurekalert.org/pub_releases/2013-11/uoha-hpp110813.php)

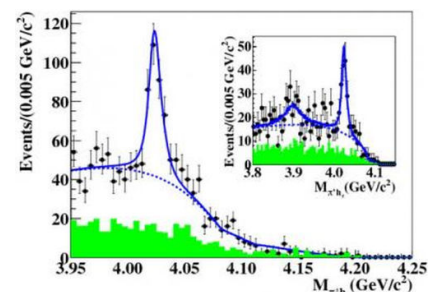
## High-energy physicists predict new family of four-quark objects

### *New charged charmonium-like states observed at BESIII*

An international team of high-energy physicists says the discovery of an electrically charged subatomic particle called  $Z_c(4020)$  is a sign that they have begun to unveil a whole new family of four-quark objects.

The Beijing Spectrometer (BESIII) collaboration, which includes scientists from the University of Hawaii at Manoa, previously announced the discovery of a mysterious four-quark particle called  $Z_c(3900)$  in April 2013.

"While quarks have long been known to bind together in groups of twos or threes, these new results seem to be quickly opening the door to a previously elusive type of four-quark matter," said Frederick Harris, a professor of physics and astronomy at UH Manoa, and a spokesman for the BESIII experiment. "The unique data sample collected by the BESIII collaboration has continued to yield a stream of clues about the nature of multi-quark objects."



### *The peak is evidence for $Z_c(4020)$ decaying to $\pi^+h_c$ . BESIII Collaboration*

The recent breakthroughs by the BESIII collaboration have come about through a dedicated study of the byproducts of the anomalous  $Y(4260)$  particle. Using the Beijing Electron Positron Collider (BEPCII) in China, scientists tuned the energy at which electrons and positrons annihilate matter to 4260 MeV, which corresponds to the mass of the  $Y(4260)$  particle. The BESIII Collaboration used this method to directly produce and collect large samples of the particle's byproducts, or decays.

This experimental method allowed the BESIII collaboration to first observe the  $Z_c(3900)$  and then the  $Z_c(4020)$ . Also recently spotted in the decays is the electrically neutral  $X(3872)$ , a particle that has been experimentally established for more than 10 years, and has long been suspected to be a four-quark object.



"The year 2013 has so far been an exciting one for the BESIII experiment," Harris said. "Using decays of the  $Y(4260)$ , a family of four-quark objects has begun to appear. While the theoretical picture remains to be finalized, more and more clues are suggesting that we are witnessing new forms of matter. And while a new 'zoo' of mysterious particles is emerging, it seems a new classification system may soon be at hand to understand it."

*About the BESIII Experiment:*

*The Beijing Spectrometer (BESIII) experiment at the Beijing Electron Positron Collider is composed of about 350 physicists from 50 institutions in 11 countries. U.S. groups include Carnegie Mellon University, Indiana University, The University of Minnesota, The University of Rochester, as well as physicists in the High Energy Physics Group, in the Department of Physics and Astronomy at the University of Hawai'i at Manoa.*

*The scientists have reported their findings to the scientific journal Physical Review Letters, including:*

*Observation of  $Z_c(4040)$  in  $e^+e^- \rightarrow D^*D^*-\pi^+$  process at 4.26 GeV arXiv:1308.2760*

*Observation of a charged charmoniumlike structure  $Z_c(4020)$  and search for the  $Z_c(3900)$  in  $e^+e^-$  to  $\pi^+\pi^-\pi^0$  arXiv:1309.1896*

*Observation of a charged  $(DD^*)$ - mass peak in  $e^+e^- \rightarrow \pi^+(DD^*)$ -at  $E_{cm}=4.26$  GeV arXiv:1310.1163*

*Observation of the  $X(3872)$  in  $e^+e^- \rightarrow \gamma \pi^+\pi^- J/\psi$  at  $\sqrt{s}$  around 4.26 GeV arXiv:1310.4101*

[http://www.eurekalert.org/pub\\_releases/2013-11/asfm-dmg110813.php](http://www.eurekalert.org/pub_releases/2013-11/asfm-dmg110813.php)

## **Drug may guard against periodontitis, and related chronic diseases**

***A drug currently used to treat intestinal worms could protect people from periodontitis***

WASHINGTON, DC - A drug currently used to treat intestinal worms could protect people from periodontitis, an advanced gum disease, which untreated can erode the structures—including bone—that hold the teeth in the jaw. The research was published ahead of print in *Antimicrobial Agents and Chemotherapy*.

Current treatment for periodontitis involves scraping dental plaque, which is a polymicrobial biofilm, off of the root of the tooth. Despite this unpleasant and costly ordeal, the biofilm frequently grows back. But the investigators showed in an animal model of periodontitis that the drug Oxantel inhibits this growth by interfering with an enzyme that bacteria require for biofilm formation, says corresponding author Eric Reynolds, of the University of Melbourne, Australia. It does so in a dose-dependent manner, indicating efficacy.

The researchers began their search for a therapy for periodontitis by studying the symbioses of the periodontal pathogens, using genomics, proteomics, and metabolomics, in animal models of periodontitis. They soon found that the periodontal biofilm depended for growth on the availability of iron and heme (an iron-containing molecule related to hemoglobin), and that restricting these reduced levels of the enzyme, fumarate reductase. Since Oxantel was known to inhibit fumarate reductase in some bacteria, they then successfully tested its ability to inhibit fumarate reductase activity in *Porphyromonas gingivalis*, one of the major bacterial components of periodontitis biofilms. Fumarate reductase is absent from humans, making it an ideal drug target.

They also showed that Oxantel disrupted the growth of polymicrobial biofilms containing *P. gingivalis*, *Tannerella forsythia*, and *Treponema denticola*, a typical composition of periodontal biofilms, despite the fact that the latter alone is unaffected by Oxantel.

The researchers found that treatment with Oxantel downregulated six *P. gingivalis* gene products, and upregulated 22 gene products, all of which are part of a regulon (a genetic unit) that controls availability of heme.

Periodontitis affects an estimated 30-47 percent of the adult population with severe forms affecting 5-10 percent. It also increases the risks of diabetes, heart disease, stroke, arthritis, and dementia, says Reynolds. These risks arise due to the pathogenic bacteria that enter the blood stream from periodontitis, as well as from the chronic inflammation caused by this disease, he says. Additionally, periodontitis correlates with increased risk of cancers of the head and neck, the esophagus, the tongue, and the pancreas, the investigators report.

The article can be found online at <http://bit.ly/asmtip1111a>.

[http://www.eurekalert.org/pub\\_releases/2013-11/m-uoc110713.php](http://www.eurekalert.org/pub_releases/2013-11/m-uoc110713.php)

## **Universals of conversation**

***Max Planck researchers found that words that signal problems with understanding are similar across languages***

A word like 'Huh?' —used when one has not caught what someone just said—appears to be universal: it is found to have very similar form and function in languages across the globe. This is one of the findings of a major cross-linguistic study by researchers Mark Dingemanse, Francisco Torreira and Nick Enfield, at the Max Planck Institute for Psycholinguistics in Nijmegen, the Netherlands. The study was published in the journal PLOS ONE.

It might seem frivolous to carry out scientific research on a word like 'Huh?' But in fact this little word is an indispensable tool in human communication. Without words like this we would be unable to signal when we

have problems with hearing or understanding what was said, and our conversations would be constantly derailed by communicative mishaps. The research is part of a larger investigation of language and social interaction funded by the European Research Council.

Dingemanse and colleagues studied languages from around the world and found that all of them have a word with a near-identical sound and function as English 'Huh?' This is remarkable because usually, words in unrelated languages sound completely different. Compare, for example, these very different-sounding words for 'dog': inu in Japanese, chien in French, dog in English. One might object that this suggests that 'Huh?' is not a word at all. But in a careful phonetic comparison, Dingemanse and colleagues find that it is. Although 'Huh?' is much more similar across languages than words normally should be, it does differ across languages in systematic ways. 'Huh?' is not like those human sounds that happen to be universal because they are innate, such as sneezing or crying. It is a word that has to be learned in subtly different forms in each language. Why is 'Huh?' so similar across languages? To understand this, Dingemanse and colleagues studied the specific context in which this word occurs. In human communication, when we are somehow unable to respond appropriately, we need an escape hatch: a way to quickly signal the problem. This signal has to be easy to produce in situations when you're literally at a loss to say something; and it has to be a questioning word to make clear that the first speaker must now speak again. Since these functional requirements are fundamentally the same across languages, they may cause spoken languages to converge on the same solution: a simple, minimal, quick-to-produce questioning syllable like English 'Huh?', Mandarin Chinese 'A?', Spanish 'E?', Lao 'A?', or Dutch 'He?'

The basic principle is well-known from evolutionary biology: when different species live in similar conditions they can independently evolve similar traits, a phenomenon known as convergent evolution. For example, sharks and dolphins have different evolutionary origins but similar body plans, because they live in the same aquatic environment. In the same way, Dingemanse and colleagues propose that words may converge on similar forms when they occur in strongly similar conversational 'environments'. A clear effect of this conversational ecology on the specific shape of linguistic expressions has not been observed before. Although 'Huh?' may almost seem primitive in its simplicity, a word with this function is not found in our closest evolutionary cousins. Only humans have communication systems in which complex thoughts can be expressed and communicative mishaps can be solved on the spot. Even a humble word like 'Huh?' can teach us a lot about our nature as ultrasocial animals.

#### *Original publication*

Dingemanse, Mark, Francisco Torreira, and N.J. Enfield. 2013. "Is 'Huh?' a universal word? Conversational infrastructure and the convergent evolution of linguistic items." *PLOS ONE*. doi:10.1371/journal.pone.0078273 — <http://dx.plos.org/10.1371/journal.pone.0078273>

*Research question: Is "Huh?" a universal word? And what is the explanation for its striking similarity across ten languages from five continents?*

#### **Key findings**

- 1. Huh? is not trivial. It might seem frivolous or even trivial to carry out scientific research on a word like Huh? But in fact this little word, along with others that function in similar ways (e.g., 'Sorry?' 'What?') is an indispensable tool in human communication. Without such words we would be unable to signal when we have problems with hearing or understanding what was said. Because conversation moves along so quickly, if we did not have reliable ways of signalling trouble, we would constantly fail to stay 'on the same page' in social interaction. While Huh? may seem an unlikely topic of scientific research, in fact human communication, and thus common understanding in social life, relies heavily on the use of such linguistic devices.*
- 2. Huh? is universal. We sampled languages from around the world in this study, and we found that all of them have a word with a near-identical sound and function as English Huh? This is an exception to the normal situation, namely that when words in different languages mean the same thing, they will usually sound completely different: compare, for example, these very different-sounding words for 'dog': inu in Japanese, chien in French, dog in English. Why do these differences between the sounds of words across languages occur? Because language does not impose any necessary connection between sound and meaning in words (a principle that linguists call 'the arbitrariness of the sign'). This study shows that 'Huh?' is a rare exception to this otherwise strong rule.*
- 3. Huh? is a word. An objection to our first finding might be that 'Huh?' is not a word after all. But our study finds that it is. Although the expression 'Huh?' is much more similar across languages than words normally should be, when we zoomed in and looked at the finer details, we discovered that this expression does differ across languages in subtle but systematic ways. These differences give us evidence that 'Huh?' is integrated into each linguistic system, thus supporting the view that it is, in fact, a word. Here are some of the subtle differences: In Spanish it's e?. In Dutch it often starts with /h/, as in hé. In Cha'palaa (an indigenous language of Ecuador) it has a falling tone and often starts with a glottal stop, as in ?a! Therefore: Huh? is not like those human sounds that happen to be universal because they are innate, such as sneezing or crying. It is a word that has to be learned in subtly different forms in each language.*

4. *Huh?* is not innate. '*Huh?*' may seem almost primitive in its simplicity, but in fact nothing like it is found in our closest evolutionary cousins. It's not an involuntary response like a sneeze or a cry of pain. Indeed, to have such a word, specialized for clarifying matters of understanding, only makes sense when a fully functioning cooperative system of communication (i.e., human language) is already in place — babies don't use it, infants don't use it perfectly, but children from about 5 have mastered it perfectly, along with the main structures of their grammar. If there is a plausible explanation that doesn't assume it's innate, we prefer that, on the standard scientific principle that it is best to keep to the simplest possible assumptions and explanations.

5. *Huh?* is likely shaped by convergent evolution. In conversation, we are under pressure to respond appropriately and timely to what was just said; when we are somehow unable to do this—for example, when we didn't quite catch what the other person just said—we need an escape hatch. This particular context places constraints on, and functional motivations for, the form of the word. The signal has to be something maximally simple and quick to produce in situations when we're literally at a loss to say something; and it has to be a questioning word to signal that the first speaker must now speak again. In language after language, we find a word like '*Huh?*' that fits the bill perfectly: it is a simple, minimal, quick-to-produce questioning syllable. We propose this is a form of convergent evolution in language. Convergent evolution is a phenomenon well-known from evolutionary biology. When different species live in similar conditions, they can independently evolve similar traits. In a similar way, the similarity of *huh?* across a set of widely divergent languages may be due to the fact that the constraints from its environment are the same everywhere.

#### **What did we do?**

We examined 196 instances of *huh?* extracted from recordings of informal conversation in 10 languages around the world: Siwu (a minority language spoken in Ghana), Italian, Mandarin Chinese, Spanish, Cha'palaa (a minority language spoken in Ecuador), Icelandic, Lao (spoken in Laos, Thailand, and Cambodia), Dutch, and Murriny Patha (an Australian Aboriginal language). In all of the languages, we restricted our focus to cases that occurred in exactly the same context in conversation. The technical term for this context is "other-initiated repair": a sequence in which one person says something, the other then 'initiates repair' by saying *Huh?*, and the first provides a 'repair solution', usually by repeating the thing they said before (though often with slight revisions).

We studied these audio recordings in two ways. First, we did an auditory phonetic analysis in which three linguistically-trained analysts independently scored every one of the 196 recordings on five phonetic dimensions. The instances were presented in random order and no information was provided about the language. One set of findings presented in the paper was derived from the combined results of this auditory phonetic coding. Second, we did an instrumental phonetic analysis of a subset of the data in order to verify the quality of the auditory analysis. For this we focused in on two of the languages—Spanish and Chapalaa (an indigenous minority language spoken in Ecuador)—and we compared readings of pitch, and of the first and second 'vowel formants' of each example (these provide an objective measure of the differences in sound between vowels such as 'a' versus 'i' versus 'u'). To make sure that the similarities we saw were not just due to our particular selection of ten languages (some of which are related), we also located examples of the interjection in as many additional languages as we could find — adding 21 languages to our original sample. In all of the languages we found an interjection that showed the same tight fit of form and function.

#### **What did we NOT do?**

We did NOT study *huh?* in dictionaries — many dictionaries don't list it as a word and even if they do we can't be sure of its precise phonetic form.

We did NOT look at uses of *huh?* in contexts other than 'other-initiated repair'. We know that *huh?*-like words are also used in other contexts (e.g. to pursue a response, or as a tag question at the end of an utterance). We suspect that these uses are related to the function we studied, but that would be a matter for another study.

We did NOT compare written-down versions of *huh?* across languages, nor did we rely on second-hand reports about the languages we studied. We collected almost 200 audio recordings of *huh?* (averaging about 20 per language) in our own field recordings, and we compared those auditorily and instrumentally. This was to make sure that our analysis was based on directly observed facts about what happens in real, everyday language use.

We did NOT study only *huh?*. This research is part of a larger investigation of language and social interaction in the ERC-funded project "Human Sociality and Systems of Language Use" led by Enfield. '*Huh?*' belongs to a larger set of expressions used to signal and solve communicative mishaps. Most of these expressions vary quite widely across languages. Only '*Huh?*', which is the most common generic signal of trouble we found, happens to be strongly similar everywhere — a finding which we report in this paper. If you are interested in the larger systems, we can recommend another comparative article, to appear in the scholarly journal *Studies in Language*: Dingemanse, Mark, Joe Blythe, and Tyko Dirksmeyer. in press. "Formats for other-initiation of repair across languages: An exercise in pragmatic typology." *Studies in Language*.

<http://www.sciencedaily.com/releases/2013/11/131108112244.htm>

## **In Animal Study, 'Cold Turkey' Withdrawal from Drugs Triggers Mental Decline** **Can quitting drugs without treatment trigger a decline in mental health?**

That appears to be the case in an animal model of morphine addiction. Georgetown University Medical Center researchers say their observations suggest that managing morphine withdrawal could promote a healthier mental state in people.

"Over time, drug-abusing individuals often develop mental disorders," says Italo Mocchetti, PhD, a professor of neuroscience. "It's been thought that drug abuse itself contributes to mental decline, but our findings suggest that 'quitting cold turkey' can also lead to damage."

In the study published in the November issue of *Brain, Behavior and Immunity* and presented at Neuroscience 2013, Mocchetti and his research colleagues treated the animals with morphine, or allowed them to undergo withdrawal by stopping the treatment. Then, they measured pro-inflammatory cytokines, which can promote damage and cell death, and the protein CCL5, which has various protective effects in the brain.

"Interestingly, we found that treating the addicted animals with morphine both increased the protective CCL5 protein while decreasing pro-inflammatory cytokines, suggesting a beneficial effect," Mocchetti explains. The animals that weren't treated during withdrawal had the opposite results -- decreased CCL5 and increased levels of the damaging cytokines.

"From these findings, it appears that morphine withdrawal may be a causative factor that leads to mental decline, presenting an important avenue for research in how we can better help people who are trying to quit using drugs," concludes Mocchetti.

*Lee A. Campbell, Valeriya Avdoshina, Summer Rozzi, Italo Mocchetti. CCL5 and cytokine expression in the rat brain: Differential modulation by chronic morphine and morphine withdrawal. Brain, Behavior, and Immunity, 2013; 34: 130 DOI: 10.1016/j.bbi.2013.08.006*

<http://www.livescience.com/41061-moon-crash-earth-magma-ocean.html>

## Early Earth May Have Spawned Magma Ocean

*Billions of years ago, the Earth's atmosphere an opaque and the planet's surface was a vast magma ocean devoid of life.*

by Katia Moskvitch, SPACE.com Contributor | November 08, 2013 01:18pm ET

LONDON - This scenario, says Stanford University professor of geophysics Norman Sleep, was what the early Earth looked like just after a cataclysmic impact by a planet-size object that smashed into the infant Earth 4.5 billion years ago and formed the moon. The moon, once fully formed, which would have appeared much larger in the sky at the time, since it was closer to Earth

Hundreds of millions of years later, he added, the first forms of life appeared, possibly having hitched a ride on a rock from Mars. The scenario is one presented by Sleep at a recent Royal Society conference here called Origin of the Moon. A paper detailing Sleep's study was submitted to the symposium volume.

Although many elements of the theory have been around for some time, Sleep's synthesis is "like putting together a jigsaw puzzle with some pieces already known and some that are speculative and have new aspects," said Dave Stevenson, a Caltech professor of planetary science who was not involved with Sleep's study.

One of these new aspects is how Earth cooled down to the temperatures necessary for life to evolve, following the — presumed — giant impact that formed the moon.

The processes Sleep discussed took place in the period called Hadean, about 4 billion to 4.5 billion years ago — before the first organisms came into being, and well before more complex life-forms, including dinosaurs, started roaming the Earth. Back then, the Earth was nothing like the blue Earth we know today.

### Scorching world

Instead, the entire Earth was hot and molten all the way to its inner core, a mixture of molten rock and liquid. No life would have been able to survive these brutally high temperatures, which reached 2,000 degrees Celsius (more than 3,600 degrees Fahrenheit). Liquid water had no chance to form.

The Earth's atmosphere at this time was also much heavier. Its mass was similar to that of today's oceans, and it pushed down on Earth's surface with a pressure of hundreds of bars. (For comparison, the average pressure at the Earth's surface today is 1 bar). It was also opaque — "you would not have been able to see much, just clouds covering everything," Stevenson said.

Beneath the clouds, a magma ocean swayed, with partially molten rock pushed around by tides, Sleep thinks. These tides were due to the mutual attraction of the Earth and the moon, and were much stronger than those in today's watery oceans, as the moon was sitting much, much closer to the Earth back then.

The tides constantly stirred the ocean, causing the mantle to lose heat, similar to stirring and blowing on a bowl of soup. But once released from the Earth's depths, the heat was trapped at the surface, held back by the thick, opaque primordial atmosphere. The heat could only escape the planet (and cool it down) at so-called cloud-top temperature levels — where it would be as cold as on a modern high mountain summit. But for the first 10 million years, the temperatures were much, much higher, Sleep said.

The energy loss caused by the mutual attraction of the Earth and the moon was also making the moon gradually pull away. This made the tides progressively weaker, so the molten rock was being stirred less and less, and the Earth's mantle began to solidify in stages.



"While at the top of the Earth there was still partially molten slurry with a bit of liquid left, in the middle there was a mushy layer, but the deep mantle was becoming solid," Sleep said. "Lava was probably still coming up and erupting and freezing at the top, and then falling back in large, kilometer-size pieces that were sinking into the Earth."

Slowly, the internal heat flow ceased to dominate the climate, and the temperatures at the surface began to drop, with the heat being able to escape the atmosphere at last.

### **Life from Mars?**

The sweltering temperatures and trapped heat were not the only obstacles for life to appear, Sleep said. Another issue was overabundance of carbon dioxide in the primordial atmosphere. Carbon dioxide doesn't dissolve in molten rock, so it was bound to bubble up from the magma ocean, creating a so-called runaway greenhouse effect, Sleep said.

For the Earth to become habitable, most of this carbon dioxide had to vanish.

Sleep said this happened when the tectonic plates began to move in the late Hadean, some 4.4 billion years ago. With the plates moving, the carbon dioxide began to enter the mantle in a process called subduction, when one tectonic plate moves under another and sinks into the mantle.

Liquid water oceans had already begun to condense around that time, and once the Earth cooled sufficiently and most of the carbon dioxide was safely tucked away in the mantle, life did finally appear, Sleep said, adding that chances are that this life arrived on Earth from Mars.

"We know life was present on Earth about 3.9 billion years ago, but Mars was probably habitable for a long time before the Earth," Sleep said. "So you had hundreds of millions of years when Mars was not a particularly unpleasant place, with liquid water. If life evolved on Mars, rocks get knocked off by asteroids all the time — so at some point, a rock from Mars could've come in, trying to hit us on the head."

And if conditions on Earth were just right for life to start, this Martian rock could've been the beginning of everything we know today. But it's still only an idea, but a testable one. Unlike Earth, though, the ancient geological record exists on Mars, Sleep said. It is just hard to examine.

<http://bit.ly/1gAwqe8>

### **Listen up: new tool to help people who are locked in**

*People who are paralysed and unable to speak may soon be able to communicate simply by focusing on voices saying "yes" or "no" while their brain is monitored.*

15:15 09 November 2013 by Alyssa Botelho

"Locked-in syndrome", can be the result of motor neurone (Lou Gehrig's) disease, multiple sclerosis or a devastating brain injury. People who are locked in often communicate via tiny eye movements or facial twitches. But sometimes even this may be impossible. Soon they may be able to communicate just by listening. Neuroscientist Jeremy Hill aims to use hearing to open up lines of communication for even these most isolated patients. He and his team at the New York State Department of Health have developed a new brain-computer interface. It can detect if someone is paying attention to one spoken word or another by measuring the pattern of electrical activity in the brain.

In the new system, users wear headphones and listen to alternating voices: a male saying "no" in the left ear, and a female saying "yes" in the right. The act of paying attention to the "yes" voice over the "no" produces a distinct electrical brainwave pattern. That can be picked up by electrodes on the scalp, and translated by Hill's algorithms to create a computerised "yes" output.

"Listening is a very private mental act that doesn't necessarily have an outward sign," says Hill, who presented this work at the 2013 Society for Neuroscience conference in San Diego. "But with this brain-computer interface we're finding that listening can become an act that influences the world in a very direct way."

Ears never get tired

In previous studies, Hill and his team used two different beeps, instead of voices, as stimuli. But subjects complained the beeps were unpleasant and sometimes difficult to match to the response they wished to convey. Hill hopes that this latest approach takes the interface closer to becoming an everyday device.

In the latest work, they tested the new system on 14 healthy volunteers. They found that on average, the algorithms had an accuracy of about 76 per cent. And responses from two people with advanced Lou Gehrig's disease were processed just as well.

Though assistive technologies using visual responses such as eye movement are more versatile than auditory ones at the moment, this could add one more tool to ease communication for people who are locked in, Hill says. He cites one Lou Gehrig's user in the study, who normally communicates via eyebrow movements, welcoming the approach and telling researchers: "My eyes get tired, but never my ears."

Hill's team is now developing an app to allow a smartphone to sync with the system.

Locked-in syndrome expert Steven Laureys of the University of Liege in Belgium is supportive of the new approach. "I think it's very important to offer alternative tools that do not depend on eye movements. We need to adapt to the specific sensory impairments of each individual patient," he says.

<http://nyti.ms/1axBmIo>

### **Work Up a Sweat, and Bargain Better**

*If better health isn't enough incentive to take a brisk walk, perhaps there is another one: it may get you a better deal.*

By MATT RICHTEL

New research from the Massachusetts Institute of Technology offers a twist on the adage "never let them see you sweat," says Jared Curhan, associate professor of organization studies at M.I.T.'s Sloan School of Management, and one of the study's co-authors. "If you're sweating, and your heart rate is up, it's seen as a sign something is going wrong, that you're too nervous, off-balance, flustered," he said. "Whereas we're showing that something could be very right."

Professor Curhan and his colleagues found that a person who negotiates while moving — say, pacing while bargaining over job terms on the cellphone — can see improved results. But there is, of course, a rub. The better outcomes seen with exertion tend to come only to people who are confident heading into the negotiation in the first place. If, instead, they are nervous, walking may actually hamper performance.

The study, published recently in the journal *Psychological Science*, involved two experiments. One compared the experience of subjects who negotiated to buy a car on a cellphone while walking briskly on a treadmill (their heart rates averaged 117 beats a minute) against the experience of others who walked at a more modest pace (88 beats a minute). A second experiment compared the experiences of subjects negotiating for job terms on a cellphone; some subjects took a casual walk, while others sat in a chair.

As conventional wisdom would suggest, those who dreaded negotiation performed even worse when they exerted themselves. What was more surprising was that those who looked forward to negotiation displayed the opposite results: In the job-negotiation experiment, they performed better and felt better about their performances when they were walking. And in the treadmill experiment, the confident negotiators felt that they performed better when their heart rates were elevated — more so than equally confident people who walked at a modest pace.

The results provide a real-world application to a decades-old body of science about the relationship between physical and mental states. It turns out that it's very easy to confuse the two. That is because, broadly speaking, emotions consist of two factors: a physiological response and how a person experiences and labels it.

In other words, one person might call a racing heart and sweaty palms anxiety and another might call it excitement. Recent research from Alison Wood Brooks, a scholar now at the Harvard Business School, shows that people perform better in a range of pursuits — singing, public speaking, math — if they can take note of the physiological responses and relabel their feelings as excitement as opposed to anxiety.

Ms. Brooks said the research would apply to negotiation. Her advice is for people to "reappraise" anxiety as excitement. This can be accomplished, she said, even by simply saying "I'm excited." Earlier research shows that anxiety can be so debilitating that it causes people to "make low first offers, exit early and earn less profit." She said the new M.I.T. research showed a way to counter these forces.

"Get on the treadmill, get your heart racing and once it's racing, appraise the feeling as excitement — tell yourself 'I am excited, not anxious,'" she said. "And then go forth and prosper."

One thing that is not clear from the M.I.T. study is just how much physical exertion makes sense in negotiation. For now, said Ashley Brown, the lead author of the study who is now a psychology researcher at Stanford, "I wouldn't suggest doing a marathon."

<http://bit.ly/1ayqZEL>

### **Maine sued by Big Pharma because it won't stop foreign drug imports**

*The pharmacies suing Maine to keep people from importing Canadian mail-order drugs carefully avoid using the word "profits" in their lawsuit.*

By George Chidi

Big Pharma notes that some of its members have been injured, but no specific claim of damage is made. Instead the complaint argues that Maine's new law explicitly authorizing pharmacies in Canada to export to Maine businesses and residents violates the U.S. constitution and federal law, and skirts domestic medicine regulations, "circumventing the carefully-constructed closed federal regulatory structure governing prescription drugs and thus posing serious health risks to consumers."

The plaintiffs — Maine pharmacists Charles Ouellette and Amelia Arnold, the Maine Society of Health-System Pharmacists, Retail Association of Maine, and Pharmaceutical Research and Manufacturers of America, or

PhRMA — want to stop Maine's new Importation Law, which won approval in June and took effect in October. The law allows licensed retail pharmacies in Canada, Australia, New Zealand or the United Kingdom to export prescription medicines by mail to Maine residents for personal use.

Maine's response argues that the state has no obligation to regulate pharmacies there if it chooses not to.

"Maine is free to choose not to regulate the conduct of pharmacies located in other countries – even if those pharmacies may engage in conduct that violates the FDCA," Maine's attorney general Janet Mills answered in filings defending the law in federal court.

<http://www.sciencedaily.com/releases/2013/11/131108090135.htm>

**Oral Allergy Syndrome, High Blood Pressure Medications Can Create Lethal Cocktail**  
*Oral allergy syndrome sufferers that take high blood pressure medications may experience extreme facial swelling and difficulty breathing the next time they bite into a juicy apple.*

When patients with oral allergy syndrome take angiotensin-converting enzyme (ACE) inhibitors for hypertension and congestive heart failure, they are at an increased risk for a life-threatening allergic reaction known as anaphylaxis, according to new research.

The case studies, being presented at the Annual Scientific Meeting of the American College of Allergy, Asthma and Immunology (ACAAI), found use of ACE inhibitors can cause what is known as a "priming effect" in oral allergy syndrome sufferers.

"When a sufferer's allergies are primed and they come in contact with a particular allergen, they experience a more severe than normal reaction," said allergist Denisa Ferastraoaru, MD, ACAAI member and lead study author. "Symptoms can include extreme facial swelling (angioedema) and difficulty breathing, which can lead to death in some cases."

Hay fever sufferers that experience an itchy mouth or scratchy throat after eating certain raw fruits or vegetables and some tree nuts, may have oral allergy syndrome. It is also known as pollen-food syndrome, since it is caused by cross-reacting allergens found in both pollen and raw produce.

"Sufferers can often mistake oral allergy syndrome symptoms for food allergy," said allergist David Rosenstreich, MD, ACAAI fellow and study author. "But it isn't a food allergy, and often patients can eat that food when it is cooked. For example, an individual may have a reaction to a raw apple but not to apples baked in a pie."

When allergists advised patients to avoid raw produce and switched from ACE inhibitors to angiotensin II receptor blocker (ARB) therapy, no further oral allergy symptoms occurred.

Not everyone with a pollen allergy will experience oral allergy syndrome when eating raw produce and tree nuts. However, the syndrome is commonly associated with these allergens:

**Birch Pollen:** *apple, almond, carrot, celery, cherry, hazelnut, kiwi, peach, pear, plum*

**Grass Pollen:** *celery, melons, oranges, peaches, tomato*

**Ragweed Pollen:** *banana, cucumber, melons, sunflower seeds, zucchini*

While oral allergy symptoms are typically mild, including mouth and throat discomfort, swelling and itching, it is important sufferers discuss these symptoms with their allergist because anaphylaxis can sometimes occur.

[http://www.eurekalert.org/pub\\_releases/2013-11/sfn-rrn110413.php](http://www.eurekalert.org/pub_releases/2013-11/sfn-rrn110413.php)

**Research reveals new understanding, warning signs, and potential treatments for multiple sclerosis**

*Scientists are gaining a new level of understanding of multiple sclerosis (MS) that may lead to new treatments and approaches to controlling the chronic disease*

SAN DIEGO - Scientists are gaining a new level of understanding of multiple sclerosis (MS) that may lead to new treatments and approaches to controlling the chronic disease, according to new research released today at Neuroscience 2013, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

MS is a severe, often crippling, autoimmune disease caused by the body's immune system attacking the nervous system. Today, more than two million people worldwide suffer from MS and other neuroinflammatory diseases. MS usually strikes in early adulthood and manifests with symptoms including vision loss, paralysis, numbness, and fatigue. The disease can be intermittent or progressive and currently has no cure.

Today's new findings show that:

*Scientists are one step closer to understanding how antibodies in the blood stream break past the brain's protective barrier to attack the optic nerves, spinal cord, and brain, causing the symptoms of neuromyelitis optica, a rare disease*

*similar to MS. Understanding how the antibodies bypass the protective blood-brain barrier could provide new approaches to treating the disease (Yukio Takeshita, MD, PhD, abstract 404.09, see attached summary).*

*A protein involved in blood clotting might serve as an early detection method for MS before symptoms occur. Early detection of the disease could lead to more effective early treatments (Katerina Akassoglou, PhD, abstract 404.11, see attached summary).*

*Low levels of a cholesterol protein correlate with the severity of a patient's MS in both human patients and mouse models. The finding suggests the protein, known to protect against inflammation, may protect against developing MS, and possibly even aid in the regeneration of damaged neurons. This research opens the door to cholesterol drugs as a possible new avenue for MS treatment (Lidia Gardner, PhD, abstract 404.01, see attached summary).*

Other recent findings discussed show that:

*A type of immune system cell has been found to directly target and damage nerve cell axons, a hallmark of MS. This may reveal a target for new therapies (Brian Sauer, PhD, presentation 404.06, see attached speaker summary).*

*While no treatments to rebuild cells damaged by MS currently exist, scientists have found that when exosomes — tiny, naturally occurring "nanovesicles" — are produced by dendritic cells and applied to the brain, they can deliver a mixture of proteins and RNAs that promote regeneration of protective myelin sheaths and guard against MS symptoms (Richard Kraig, MD, PhD, presentation 812.02, see attached speaker summary).*

"The findings shown today represent real promise for the millions suffering from MS," said press conference moderator Jeffrey Rothstein of Johns Hopkins University and an expert in neurodegenerative diseases. "These studies are breakthroughs in understanding and treating a disease that remains uncured, difficult to diagnose, and for which it is very difficult to prevent progression."

*This research was supported by national funding agencies such as the National Institutes of Health, as well as private and philanthropic organizations. Find more information on MS at [BrainFacts.org](http://BrainFacts.org).*