

## **High blood caffeine levels in older adults linked to avoidance of Alzheimer's disease** ***Those cups of coffee that you drink every day to keep alert appear to have an extra perk – especially if you're an older adult.***

Tampa, FL - A recent study monitoring the memory and thinking processes of people older than 65 found that all those with higher blood caffeine levels avoided the onset of Alzheimer's disease in the two-to-four years of study follow-up. Moreover, coffee appeared to be the major or only source of caffeine for these individuals. Researchers from the University of South Florida ([www.usf.edu](http://www.usf.edu)) and the University of Miami ([www.miami.edu](http://www.miami.edu)) say the case control study provides the first direct evidence that caffeine/coffee intake is associated with a reduced risk of dementia or delayed onset. Their findings will appear in the online version of [an article to be published June 5](#) in the Journal of Alzheimer's Disease, published by IOS Press. The collaborative study involved 124 people, ages 65 to 88, in Tampa and Miami.

"These intriguing results suggest that older adults with mild memory impairment who drink moderate levels of coffee -- about 3 cups a day -- will not convert to Alzheimer's disease -- or at least will experience a substantial delay before converting to Alzheimer's," said study lead author Dr. Chuanhai Cao, a neuroscientist at the USF College of Pharmacy (<http://health.usf.edu/nocms/pharmacy/>) and the USF Health Byrd Alzheimer's Institute (<http://health.usf.edu/nocms/byrd/>). "The results from this study, along with our earlier studies in Alzheimer's mice, are very consistent in indicating that moderate daily caffeine/coffee intake throughout adulthood should appreciably protect against Alzheimer's disease later in life."

The study shows this protection probably occurs even in older people with early signs of the disease, called mild cognitive impairment, or MCI. Patients with MCI already experience some short-term memory loss and initial Alzheimer's pathology in their brains. Each year, about 15 percent of MCI patients progress to full-blown Alzheimer's disease. The researchers focused on study participants with MCI, because many were destined to develop Alzheimer's within a few years. Blood caffeine levels at the study's onset were substantially lower (51 percent less) in participants diagnosed with MCI who progressed to dementia during the two-to-four year follow-up than in those whose mild cognitive impairment remained stable over the same period.

No one with MCI who later developed Alzheimer's had initial blood caffeine levels above a critical level of 1200 ng/ml – equivalent to drinking several cups of coffee a few hours before the blood sample was drawn. In contrast, many with stable MCI had blood caffeine levels higher than this critical level.

"We found that 100 percent of the MCI patients with plasma caffeine levels above the critical level experienced no conversion to Alzheimer's disease during the two-to-four year follow-up period," said study co-author Dr. Gary Arendash.

The researchers believe higher blood caffeine levels indicate habitually higher caffeine intake, most probably through coffee. Caffeinated coffee appeared to be the main, if not exclusive, source of caffeine in the memory-protected MCI patients, because they had the same profile of blood immune markers as Alzheimer's mice given caffeinated coffee. Alzheimer's mice given caffeine alone or decaffeinated coffee had a very different immune marker profile.

Since 2006, USF's Dr. Cao and Dr. Arendash have published several studies investigating the effects of caffeine/coffee administered to Alzheimer's mice. Most recently, they reported that caffeine interacts with a yet unidentified component of coffee to boost blood levels of a critical growth factor that seems to fight off the Alzheimer's disease process. "We are not saying that moderate coffee consumption will completely protect people from Alzheimer's disease," Dr. Cao cautioned. "However, we firmly believe that moderate coffee consumption can appreciably reduce your risk of Alzheimer's or delay its onset."

Alzheimer's pathology is a process in which plaques and tangles accumulate in the brain, killing nerve cells, destroying neural connections, and ultimately leading to progressive and irreversible memory loss. Since the neurodegenerative disease starts one or two decades before cognitive decline becomes apparent, the study authors point out, any intervention to cut the risk of Alzheimer's should ideally begin that far in advance of symptoms.

"Moderate daily consumption of caffeinated coffee appears to be the best dietary option for long-term protection against Alzheimer's memory loss," Dr. Arendash said. "Coffee is inexpensive, readily available, easily gets into the brain, and has few side-effects for most of us. Moreover, our studies show that caffeine and coffee appear to directly attack the Alzheimer's disease process."

In addition to Alzheimer's disease, moderate caffeine/coffee intake appears to reduce the risk of several other diseases of aging, including Parkinson's disease, stroke, Type II diabetes, and breast cancer. However,

supporting studies for these benefits have all been observational (uncontrolled), and controlled clinical trials are needed to definitively demonstrate therapeutic value.

A study tracking the health and coffee consumption of more than 400,000 older adults for 13 years, and published earlier this year in the *New England Journal of Medicine*, found that coffee drinkers reduced their risk of dying from heart disease, lung disease, pneumonia, stroke, diabetes, infections, and even injuries and accidents.

With new Alzheimer's diagnostic guidelines encompassing the full continuum of the disease, approximately 10 million Americans now fall within one of three developmental stages of Alzheimer's disease -- Alzheimer's disease brain pathology only, MCI, or diagnosed Alzheimer's disease. That number is expected to climb even higher as the baby-boomer generation continues to enter older age, unless an effective and proven preventive measure is identified. "If we could conduct a large cohort study to look into the mechanisms of how and why coffee and caffeine can delay or prevent Alzheimer's disease, it might result in billions of dollars in savings each year in addition to improved quality of life," Dr. Cao said.

*The USF-UM study was funded by the NIH-designated Florida Alzheimer's Disease Research Center and the State of Florida.*

[http://www.eurekalert.org/pub\\_releases/2012-06/afot-ajh060412.php](http://www.eurekalert.org/pub_releases/2012-06/afot-ajh060412.php)

### **Ancient jugs hold the secret to practical mathematics in Biblical times**

#### ***Precise volume was measured by circumference, Tel Aviv University researchers find***

Archaeologists in the eastern Mediterranean region have been unearthing spherical jugs, used by the ancients for storing and trading oil, wine, and other valuable commodities. Because we're used to the metric system, which defines units of volume based on the cube, modern archaeologists believed that the merchants of antiquity could only approximately assess the capacity of these round jugs, says Prof. Itzhak Benenson of Tel Aviv University's Department of Geography. Now an interdisciplinary collaboration between Prof. Benenson and Prof. Israel Finkelstein of TAU's Department of Archaeology and Ancient Near Eastern Cultures has revealed that, far from relying on approximations, merchants would have had precise measurements of their wares — and therefore known exactly what to charge their clients.

The researchers discovered that the ancients devised convenient mathematical systems in order to determine the volume of each jug. They theorize that the original owners and users of the jugs measured their contents through a system that linked units of length to units of volume, possibly by using a string to measure the circumference of the spherical container to determine the precise quantity of liquid within.

The system, which the researchers believe was developed by the ancient Egyptians and used in the Eastern Mediterranean from about 1,500 to 700 BCE, was recently reported in the journal *PLoS ONE*. Its discovery was part of the Reconstruction of Ancient Israel project supported by the European Union.

#### **3D models unveil volume measurement system**

The system of measurement was revealed when mathematician Elena Zapassky constructed 3D models of jugs from Tel Megiddo — an important Canaanite city-state and Israelite administration center — for a computer database. The jugs are associated with the Phoenicians, ancient seafaring merchants who had trading hubs along the coast of Lebanon. Using a statistical methodology, the team measured hundreds of vessels from the excavation, and discovered something surprising — large groups of these spherical or elliptic jugs had a similar circumference. This prompted the researchers to look more deeply into how the ancients measured volume.

The Egyptian unit of volume is called the hekat, and it equals 4.8 liters in today's measurements, explains Dr. Yuval Gadot, a researcher on the project. A spherical jug that is 52 centimeters in circumference, which equals one Egyptian royal cubit, contains exactly half a hekat. "In a large percentage of the vessels we measured, the circumference is close to one cubit, and the merchant could know that the vessel's volume is half a cubit by just measuring its circumference," he says.

When the researchers adopted the Egyptian system of measurement themselves instead of thinking in metrical units, many things became clear. For example, the tall round "torpedo" jugs packed into Phoenician ships in the 8th century BCE were found to contain whole units of hekats. Dr. Gadot believes that the Egyptian system of measurement gradually disappeared when the Assyrians took over the region, bringing their own methods of measurement with them.

#### **A measure of political power**

According to Prof. Finkelstein, elements of standardization in the ancient world hold interest because they are indicative of bureaucratic systems and reflect political and cultural influences. "The use of the Egyptian method is a strong indicator of Egyptian power in this region during a specific period of time," he explains.

"Working together with experts in mathematics and statistics, we have been able to provide new solutions for longstanding archaeological problems and debates."

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## **Reign of the giant insects ended with the evolution of birds**

***Giant insects ruled the prehistoric skies during periods when Earth's atmosphere was rich in oxygen. Then came the birds.***

SANTA CRUZ, CA- After the evolution of birds about 150 million years ago, insects got smaller despite rising oxygen levels, according to a new study by scientists at the University of California, Santa Cruz.

Insects reached their biggest sizes about 300 million years ago during the late Carboniferous and early Permian periods. This was the reign of the predatory griffinflies, giant dragonfly-like insects with wingspans of up to 28 inches (70 centimeters). The leading theory attributes their large size to high oxygen concentrations in the atmosphere (over 30 percent, compared to 21 percent today), which allowed giant insects to get enough oxygen through the tiny breathing tubes that insects use instead of lungs.

The new study takes a close look at the relationship between insect size and prehistoric oxygen levels. Matthew Clapham, an assistant professor of Earth and planetary sciences at UC Santa Cruz, and Jered Karr, a UCSC graduate student who began working on the project as an undergraduate, compiled a huge dataset of wing lengths from published records of fossil insects, then analyzed insect size in relation to oxygen levels over hundreds of millions of years of insect evolution. Their findings are published in the June 4 online early edition of the Proceedings of the National Academy of Sciences (PNAS).

"Maximum insect size does track oxygen surprisingly well as it goes up and down for about 200 million years," Clapham said. "Then right around the end of the Jurassic and beginning of the Cretaceous period, about 150 million years ago, all of a sudden oxygen goes up but insect size goes down. And this coincides really strikingly with the evolution of birds." With predatory birds on the wing, the need for maneuverability became a driving force in the evolution of flying insects, favoring smaller body size.

The findings are based on a fairly straightforward analysis, Clapham said, but getting the data was a laborious task. Karr compiled the dataset of more than 10,500 fossil insect wing lengths from an extensive review of publications on fossil insects. For atmospheric oxygen concentrations over time, the researchers relied on the widely used "Geocarbsulf" model developed by Yale geologist Robert Berner. They also repeated the analysis using a different model and got similar results.

The study provided weak support for an effect on insect size from pterosaurs, the flying reptiles that evolved in the late Triassic about 230 million years ago. There were larger insects in the Triassic than in the Jurassic, after pterosaurs appeared. But a 20-million-year gap in the insect fossil record makes it hard to tell when insect size changed, and a drop in oxygen levels around the same time further complicates the analysis.

Another transition in insect size occurred more recently at the end of the Cretaceous period, between 90 and 65 million years ago. Again, a shortage of fossils makes it hard to track the decrease in insect sizes during this period, and several factors could be responsible. These include the continued specialization of birds, the evolution of bats, and a mass extinction at the end of the Cretaceous.

"I suspect it's from the continuing specialization of birds," Clapham said. "The early birds were not very good at flying. But by the end of the Cretaceous, birds did look quite a lot like modern birds."

Clapham emphasized that the study focused on changes in the maximum size of insects over time. Average insect size would be much more difficult to determine due to biases in the fossil record, since larger insects are more likely to be preserved and discovered.

"There have always been small insects," he said. "Even in the Permian when you had these giant insects, there were lots with wings a couple of millimeters long. It's always a combination of ecological and environmental factors that determines body size, and there are plenty of ecological reasons why insects are small."

*This research was supported by the National Science Foundation and UC Santa Cruz.*

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## **How infectious disease may have shaped human origins**

***Inactivation of 2 genes may have allowed escape from bacterial pathogens, researchers say***

Roughly 100,000 years ago, human evolution reached a mysterious bottleneck: Our ancestors had been reduced to perhaps five to ten thousand individuals living in Africa. In time, "behaviorally modern" humans would emerge from this population, expanding dramatically in both number and range, and replacing all other co-existing evolutionary cousins, such as the Neanderthals. The cause of the bottleneck remains unsolved, with proposed answers ranging from gene mutations to cultural developments like language to climate-altering events, among them a massive volcanic eruption. Add another possible factor: infectious disease.

In a paper published in the June 4, 2012 online Early Edition of The Proceedings of the National Academy of Sciences, an international team of researchers, led by scientists at the University of California, San Diego

School of Medicine, suggest that inactivation of two specific genes related to the immune system may have conferred selected ancestors of modern humans with improved protection from some pathogenic bacterial strains, such as Escherichia coli K1 and Group B Streptococci, the leading causes of sepsis and meningitis in human fetuses, newborns and infants.

"In a small, restricted population, a single mutation can have a big effect, a rare allele can get to high frequency," said senior author Ajit Varki, MD, professor of medicine and cellular and molecular medicine and co-director of the Center for Academic Research and Training in Anthropogeny at UC San Diego. "We've found two genes that are non-functional in humans, but not in related primates, which could have been targets for bacterial pathogens particularly lethal to newborns and infants. Killing the very young can have a major impact upon reproductive fitness. Species survival can then depend upon either resisting the pathogen or on eliminating the target proteins it uses to gain the upper hand."

In this case, Varki, who is also director of the UC San Diego Glycobiology Research and Training Center, and colleagues in the United States, Japan and Italy, propose that the latter occurred. Specifically, they point to inactivation of two sialic acid-recognized signaling receptors (siglecs) that modulate immune responses and are part of a larger family of genes believed to have been very active in human evolution.

Working with Victor Nizet, MD, professor of pediatrics and pharmacy, Varki's group had previously shown that some pathogens can exploit siglecs to alter the host immune responses in favor of the microbe. In the latest study, the scientists found that the gene for Siglec-13 was no longer part of the modern human genome, though it remains intact and functional in chimpanzees, our closest evolutionary cousins. The other siglec gene – for Siglec-17 – was still expressed in humans, but it had been slightly tweaked to make a short, inactive protein of no use to invasive pathogens. "Genome sequencing can provide powerful insights into how organisms evolve, including humans," said co-author Eric D. Green, MD, PhD, director of the National Human Genome Research Institute at the National Institutes of Health.

In a novel experiment, the scientists "resurrected" these "molecular fossils" and found that the proteins were recognized by current pathogenic strains of E. coli and Group B Streptococci. "The modern bugs can still bind and could potentially have altered immune reactions," Varki said.

Though it is impossible to discern exactly what happened during evolution, the investigators studied molecular signatures surrounding these genes to hypothesize that predecessors of modern humans grappled with a massive pathogenic menace between 100,000 and 200,000 years ago. This presumed "selective sweep" would have devastated their numbers. Only individuals with certain gene mutations survived – the tiny, emergent population of anatomically modern humans that would result in everyone alive today possessing a non-functional Siglec-17 gene and a missing Siglec-13 gene. Varki said it's probable that humanity's evolutionary bottleneck was the complex result of multiple, interacting factors. "Speciation (the process of evolving new species from existing ones) is driven by many things," he said. "We think infectious agents are one of them." *Co-authors of the paper include Xiaoxia Wang, Ismael Secundino, Nivedita Mitra, Kalyan Banda, Vered Padler-Karavani, Andrea Verhagen and Chris Reid, Victor Nizet and Jack D. Bui, Departments of Medicine, Cellular and Molecular Medicine, Pathology and Pediatrics, UC San Diego and the UC San Diego Glycobiology Research and Training Center; the Skaggs School of Pharmacy and Pharmaceutical Sciences and UC San Diego /Salk Center for Academic Research and Training in Anthropogeny; Martina Lari, Carlotta Balsamo and David Caramelli, Department of Evolutionary Biology, Laboratory of Anthropology, University of Florence; Ermanno Rizzi, Giorgio Corti, Gianluca De Bellis, Institute for Biomedical Technologies, National Research Council, Italy; Laura Longo, Department of Environmental Science, University of Siena, Italy; William Beggs and Sarah Tishkoff, Departments of Genetics and Biology, University of Pennsylvania; Toshiyuki Hayakawa, Primate Research Institute, Kyoto University; Pedro Cruz, Eric D. Green and James C. Mullikin, National Human Genome Research Institute, National Institutes of Health.*

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**Ginseng fights fatigue in cancer patients, Mayo Clinic-led study finds**  
***High doses of the herb American ginseng over two months reduced cancer-related fatigue in patients more effectively than a placebo***

ROCHESTER, Minn. - High doses of the herb American ginseng (*Panax quinquefolius*) over two months reduced cancer-related fatigue in patients more effectively than a placebo, a Mayo Clinic-led study found. Sixty percent of patients studied had breast cancer. Researchers studied 340 patients who had completed cancer treatment or were being treated for cancer at one of 40 community medical centers. Each day, participants received a placebo or 2,000 milligrams of ginseng administered in capsules containing pure, ground American ginseng root. The findings are being presented at the American Society of Clinical Oncology's annual meeting.

"Off-the-shelf ginseng is sometimes processed using ethanol, which can give it estrogen-like properties that may be harmful to breast cancer patients," says researcher Debra Barton, Ph.D., of the Mayo Clinic Cancer Center.

At four weeks, the pure ginseng provided only a slight improvement in fatigue symptoms. However, at eight weeks, ginseng offered cancer patients significant improvement in general exhaustion — feelings of being "pooped," "worn out," "fatigued," "sluggish," "run-down," or "tired" — compared to the placebo group.

"After eight weeks, we saw a 20-point improvement in fatigue in cancer patients, measured on a 100-point, standardized fatigue scale," Dr. Barton says. The herb had no apparent side effects, she says.

Ginseng has long been used in traditional Chinese medicine as a natural energy booster. Until this study, its effects had not been tested extensively against the debilitating fatigue that occurs in up to 90 percent of cancer patients. Fatigue in cancer patients has been linked to an increase in the immune system's inflammatory cytokines as well as poorly regulated levels of the stress-hormone cortisol. Ginseng's active ingredients, called ginsenosides, have been shown in animal studies to reduce cytokines related to inflammation and help regulate cortisol levels.

Dr. Barton's next study will look closely at ginseng's effects on the specific biomarkers for fatigue. "Cancer is a prolonged chronic stress experience and the effects can last 10 years beyond diagnosis and treatment," she says. "If we can help the body be better modulated throughout treatment with the use of ginseng, we may be able to prevent severe long-term fatigue."

*The study was funded by the National Cancer Institute and the Breast Cancer Research Foundation. Other authors include Breanna Linquist, and Charles Loprinzi, M.D., of Mayo Clinic; Shaker Dakhil, M.D., of Wichita Community Clinical Oncology Program; James Bearden, M.D., and Travis McGinn, of Spartanburg Regional Medical Center; Craig Nichols, M.D., of Virginia Mason Medical Center; Greg Seeger, M.D., of Altru Cancer Center; Ernie Balcueva, M.D., of Saginaw, Mich.*

<http://www.sciencedaily.com/releases/2012/06/120604093106.htm>

**Immune System Glitch Tied to Fourfold Higher Likelihood of Death Identified**  
***Mayo Clinic researchers have identified an immune system deficiency whose presence shows someone is up to four times likelier to die than a person without it.***

ScienceDaily- The glitch involves an antibody molecule called a free light chain; people whose immune systems produce too much of the molecule are far more likely to die of a life-threatening illness such as cancer, diabetes and cardiac and respiratory disease than those whose bodies make normal levels.

The study is published in the June issue of Mayo Clinic Proceedings.

Researchers studied blood samples from nearly 16,000 people 50 and older enrolled in a population-based study of plasma cell disorders in Olmsted County, Minn. They found that those who had the highest level of free light chains -- the top 10 percent -- were about four times more at risk of dying than those with lower levels. Even after accounting for differences in age, gender and kidney function, the risk of death was roughly twice as high. The study suggests that high levels of free light chains are markers of increased immune system response to infection, inflammation or some other serious disorders, says lead researcher Vincent Rajkumar, M.D., a Mayo Clinic hematologist.

Researchers have known that high levels of free light chains are associated with increased risk of death among patients with plasma disorders, such as lymphomas and other blood cancers, but this is the first study to find that high levels of light chains are associated with increased mortality in the general population. Free light chain levels can be measured by using a serum free light chain assay, a simple blood test. This test is often used to monitor light chain levels in patients with plasma disorders such as myeloma to gauge how well they are responding to treatment.

However, Dr. Rajkumar cautions against administering this test with the intent of gauging one's risk of death. "We do not recommend this test as a screening test, because it will only cause alarm," Dr. Rajkumar says. "We do not know why this marker is associated with higher rates of death. We do not have a way of turning things around. Therefore, I would urge caution in using this test until we figure out what to do about it and what these results mean."

Plasma cells are white blood cells that produce large amounts of antibodies and are key to fighting off infection. The antibodies are composed of two different types of molecules tightly joined to each other: heavy chains and light chains. Most people produce at least a slightly excess amount of light chains that can be detected in the blood in the "free" state, unbound to heavy chains. Free light chains are not usually a threat to health, but excess levels serve as a marker of underlying immune system stimulation, kidney failure or plasma cell disorders such as myeloma.

Next steps for researchers include identifying the precise mechanisms by which excess free light chains are associated with a higher likelihood of death and determining if specific diagnostic or treatment options need to be pursued.

The study was funded by the National Institutes of Health. Freelite, the manufacturer of the serum free light chain assay, provided the serum free light chain assay reagents for this study.

Angela Dispenziersi et al. *Use of Nonclonal Serum Immunoglobulin Free Light Chains to Predict Overall Survival in the General Population.* *Mayo Clin Proc*, 2012 DOI: 10.1016/j.mayocp.2012.03.009

<http://nyti.ms/LijqKR>

## **Really? Always Shave the Patient Before Surgery**

***THE FACTS "Prepping" a patient for surgery usually involves shaving areas where incisions are to be made.***

**By ANAHAD O'CONNOR**

Some surgeons believe it is important to remove anything that might obstruct their view. Others see shaving as a way to eliminate bacteria that clings to the hair and can contaminate the surgical site.

But research suggests that shaving a patient's skin before surgery may raise the risk of an infection.

According to the Centers for Disease Control and Prevention, surgical site infections are a leading cause of complications among hospital patients, accounting for nearly one out of five health care-associated infections and thousands of deaths annually.

A study published in the journal *Spine* looked at a group of patients having spinal surgery and found that while postoperative infections were low over all, they were more common among patients who were shaved for surgery than among those who were not. The reason, experts say, is that shaving with a razor blade causes microscopic nicks in the skin that can become bacterial breeding grounds.

In its guidelines for preventing surgical site infections, the C.D.C. recommends that hair not be removed unless it will interfere with the operation. When shaving is necessary, electrical clippers should be used.

One study showed that patients with shaved incision sites had a 5.6 percent rate of infection, compared with a rate of less than 1 percent among patients whose hair was removed with clippers.

**THE BOTTOM LINE** Shaving before surgery can raise the risk of a postoperative infection.

<http://www.sciencedaily.com/releases/2012/06/120604155556.htm>

## **'Good Fat' Activated by Cold, Not Ephedrine**

***Researchers at Joslin Diabetes Center have shown that while a type of "good" fat found in the body can be activated by cold temperatures, it is not able to be activated by the drug ephedrine.***

ScienceDaily - The finding, published in a recent issue of *Proceedings of the National Academy of Sciences*, may lead to drugs or other methods aimed at activating the good fat, known as brown fat. When activated, brown fat burns calories and can help in the battle against obesity.

"We propose that agents that work similarly to cold in activating brown fat specifically can provide promising approaches to fighting obesity while minimizing other side effects," said Aaron Cypess, M.D., Ph.D., an assistant investigator and staff physician at Joslin and lead author of the paper.

"At the same time, we now know that ephedrine is not the way to do it," he added.

Brown fat is found in humans naturally and consumes calories to generate heat. Prior studies had shown that brown fat can be activated by cold exposure in a process called non-shivering thermogenesis.

Researchers have been working for years to find ways to activate brown fat. Ephedrine, a decongestant and bronchodilator, has been used as a weight loss drug because it increases the number of calories burned.

However, there are side effects.

In this study, the Joslin team tested 10 study subjects in three ways. They were each separately given injections of ephedrine, given injections of saline as a control, and made to wear "cooling vests" that had water cooled to 57 degrees pumped into them. After each intervention, the brown fat activity was measured using PET/CT scans. The researchers found that brown fat activity was the same following both the ephedrine and saline injections. However, after the subjects wore the cooling vests for two hours, their brown fat activity was stimulated significantly.

Both interventions -- ephedrine injections and the wearing of the cooling vests -- did result in the same number of calories being burned, Dr. Cypess noted. "But we found that ephedrine was not using brown fat to do it," he said. "This is the first time it has been found that ephedrine does not turn on brown fat."

Both interventions had other effects on the sympathetic nervous system -- which activates the fight or flight response -- such as increased blood pressure, but those associated with brown fat activation were fewer, the study showed.

"Mild cold exposure stimulates (brown fat) energy expenditure with fewer other systemic effects, suggesting that cold activates specific sympathetic pathways," the paper concludes. "Agents that mimic cold activation of (brown fat) could provide a promising approach to treating obesity while minimizing systemic effects." As a result of the findings, drug companies may find it easier to come up with agents that stimulate brown fat to help people lose weight, Dr. Cypess said.

One method may be simply to design cooling vests that people can wear to help them lose weight. A future study will have subjects wear the vests for several weeks to see what happens, Dr. Cypess said.

"Will they get the same health benefits they would have seen with several weeks of exercise? That's the billion dollar question." The findings should also be of interest to heart researchers interested in the mechanisms of activation of the sympathetic nervous system, he added.

Co-authors of the June 4 study include Yih-Chieh Chen, Cathy Sze, Ke Wang, Jeffrey English, Onyee Chan, Ashley R. Holman, Ilan Tal, Matthew R. Palmer, Gerald M. Kolodny and C. Ronald Kahn. All are from either Joslin Diabetes Center or Beth Israel Deaconess Medical Center. The study was funded by the National Institutes of Health.

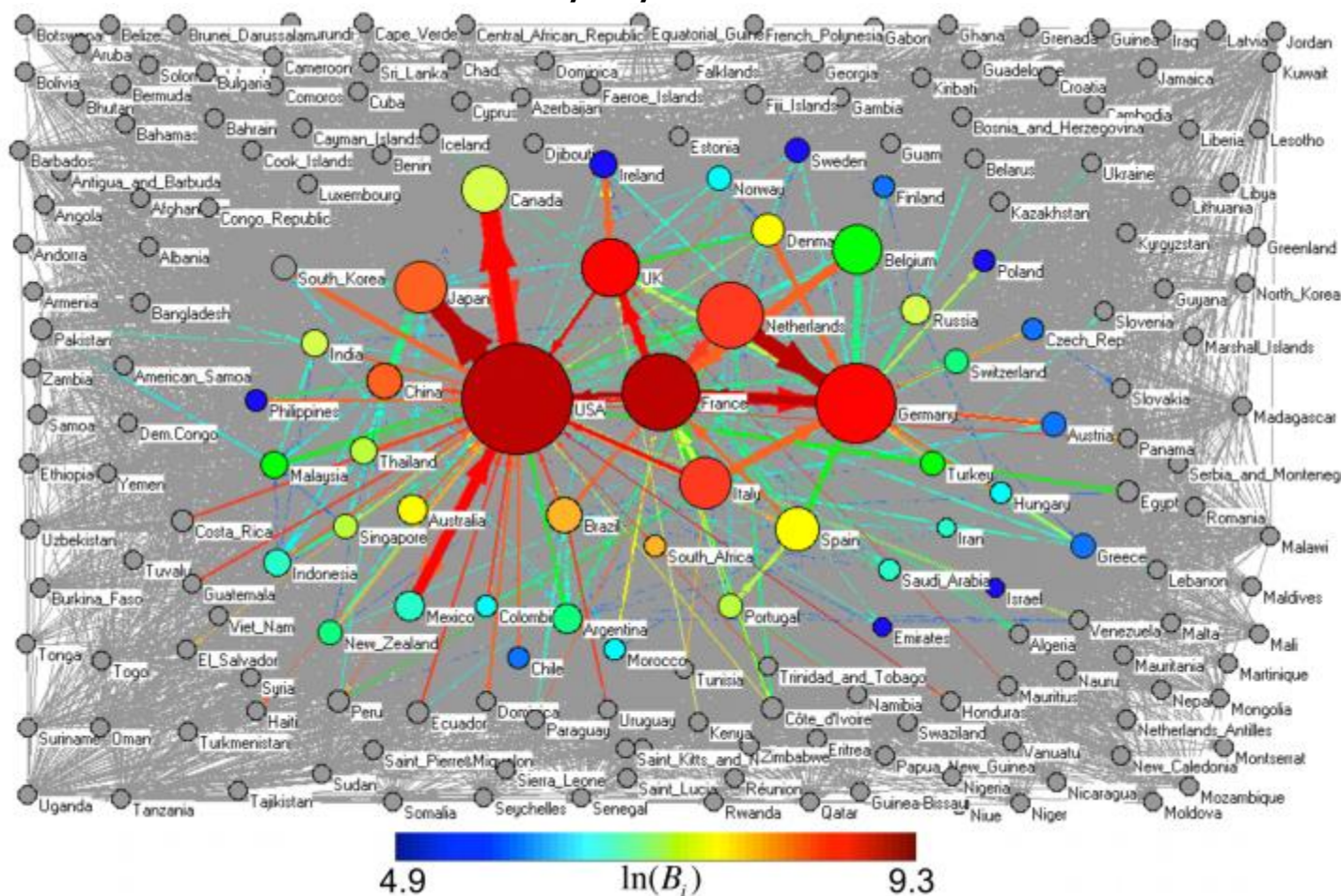
Aaron M. Cypess, Yih-Chieh Chen, Cathy Sze, Ke Wang, Jeffrey English, Onyee Chan, Ashley R. Holman, Ilan Tal, Matthew R. Palmer, Gerald M. Kolodny, and C. Ronald Kahn. Cold but not sympathomimetics activates human brown adipose tissue in vivo. *Proceedings of the National Academy of Sciences*, June 4, 2012 DOI: 10.1073/pnas.1207911109

<http://www.wired.com/wiredscience/2012/06/food-trade-complex/>

### Food Trade Too Complex To Track Food Safety

**The global trade in food has become so complex that we have almost lost the ability to trace the path of any food sold into the network.**

By Maryn McKenna



The data-dense graphic above may be too reduced to read ([here's the really big version](#)), but its intricacy masks a simple and fairly dire message: The global trade in food has become so complex that we have almost lost the ability to trace the path of any food sold into the network. And, as a result, we are also about to lose the ability to track any contaminated food, or any product causing foodborne illness.

The graphic, and warning, come from a paper [published last week in PLoS ONE](#) by researchers from the United States, United Kingdom, Hungary and Romania. The group used United Nations food-trade data — along with some math that I do not pretend to understand — to describe an “international agro-food trade network” (IFTN)

with seven countries at its center, but a dense web of connections with many others. Each of the seven countries, they find, trades with more than 77 percent of all the 207 countries on which the UN gathers information. As a result, they say: “The IFTN has become a densely interwoven complex network, creating a perfect platform to spread potential contaminants with practically untraceable origins.”

Some background facts: The current trade in food is worth \$1.06 trillion, up from \$438 billion just 10 years earlier. Food trade, in fact, has been growing faster than food production: Components made multiple trips through the system, becoming ingredients in processed foods that are assembled out of products from all over the globe.

As one example of that complexity, a [press release](#) about this study described a chicken Kiev prepared entree served in a Dublin restaurant that was found to contain ingredients from 53 countries. Remember, too, that it took weeks to track down the seeds that were the heart of the massive European E. coli outbreak last summer; when they were finally identified, they turned out to have been moving from country to country, sold and repackaged and sold again, out of a shipment that first left an Egyptian port in 2009.

The effect of that complexity is to unmoor foods from their origins, obscuring their path from original product, to ingredient, to ingredient within ingredient — and making it effectively impossible to track a contaminated or illness-causing food through its iterations down the chain.

The authors say:

*... the trends shown in (the figure above) cannot be sustained if both free trade and the demand for biotracing are to be met. During a food poisoning outbreak the first and most important task is to identify the origin of the contamination. Delays in this task can have severe consequences for the health of the population and incur social, political and economical damages with international repercussions...*

Note that our study does not predict an increase in the number of food poisoning cases but that, when it happens, there will be inevitable delays in identifying the sources due to the increasingly interwoven nature of the IFTN. That is, even if food contamination was less frequent, for example due to better local control of production, its dispersion/spread is becoming more efficient.

The paper is short and worth reading in its entirety, especially for its modelling of possible paths of hypothetical ingredients. It’s a chilling reminder, though, that if you buy any kind of processed food, you really have no way of knowing what’s in it. And even “buying local” might not protect you: The salad sprouts grown from those Egyptian seeds last year certainly seemed to be local to buyers, because they were raw, fresh and highly perishable. But the seeds they started as took a long trip to get to where they were sprouted, and as more than 3,000 sick people discovered, those seeds became contaminated in some untraceable spot along the way.

*Cite: Ercsey-Ravasz M, Toroczkai Z, Lakner Z, Baranyi J (2012) Complexity of the International Agro-Food Trade Network and Its Impact on Food Safety. PLoS ONE 7(5): e37810. doi:10.1371/journal.pone.0037810*

<http://nyti.ms/L0yhao>

## **New Epilepsy Tactic: Fight Inflammation**

***In November 2008, when he was just 6, William Moller had his first epileptic seizure, during a reading class at school.***

**By ALASTAIR GEE**

For about 20 seconds, he simply froze in place, as if someone had pressed a pause button. He could not respond to his teacher. This is known as an absence seizure, and over the next year William, now 10, who lives with his family in Brooklyn, went from having one or two a day to suffering constant seizures. Not all were absence seizures; others were frightening tonic-clonics, also known as grand mals, during which he lost consciousness and convulsed.

The seizures often came while he was eating. As his body went rigid, William dropped his food and his eyes rolled back into their sockets. If he seized while standing, he suddenly crashed to the ground — in a corridor, in the driveway, on the stairs. “It’s the scariest thing for any mother to hear that thump, and each time he would hit his head, so it only made things worse and worse,” said his mother, Elisa Moller, a pediatric nurse.

William is among the one-third of epilepsy sufferers who do not respond, or respond only poorly, to anti-epileptic medications. Now he and others with refractory epilepsy are benefiting from treatment that targets inflammation, the result of new research into how epilepsy damages the brain.

“Many of us theorize that the two are tied — inflammation causes seizures, and seizures cause inflammation,” said Orrin Devinsky, director of the Comprehensive Epilepsy Center at the New York University Langone Medical Center and William’s doctor. “Over time, both of them may feed off each other.”

About 50 million people worldwide, including more than 2.7 million people in the United States, are struggling with epilepsy in some form. Half of all patients are children. Epilepsy can result from brain injury, but in most



cases the cause is unknown and may be genetic. Refractory epilepsy, its intractable form, and the medications with which doctors attempt to treat it can cause lifelong problems with learning, memory and behavior. An epileptic seizure occurs when large groups of neurons in the brain begin firing uncontrollably, disrupting the balance of electrical activity and causing changes in mental function, motor function and behavior. It's not known what sets off a seizure, but lately scientists like Dr. Devinsky have been gathering evidence that inflammation, the immune system's response to injuries or foreign organisms, plays a pivotal role.

Scientists have known since the 1950s that inflammation is involved in a particularly vicious brain disorder called Rasmussen's encephalitis, which starts seizures and usually affects children. Inflammation inflicts such severe damage to the brain that the standard treatment for the condition is hemispherectomy — the surgical removal of one of the brain's hemispheres. Some researchers also suspect an inflammatory link to another form of epilepsy, infantile spasms, because children with the disease respond to ACTH, a hormone produced in the pituitary gland with strong anti-inflammatory effects.

Eleonora Aronica, a neuropathologist at the University of Amsterdam, has found signs of inflammation in autopsy specimens and surgical resections from patients with a wide range of epilepsies. Annamaria Vezzani, a neuroscientist at the Mario Negri Institute for Pharmacological Research in Milan, has induced epilepsy in mice and rats by injecting kainic acid into their brains, and has observed the activation of a cellular pathway linked to inflammation before and during seizures.

The amount of inflammation in the brain correlates with the frequency of seizures, she also has found. "This is a novel finding," Dr. Vezzani said in an interview. "It was not known that inflammation was a common feature of different types of epilepsy."

Normal brain function is regulated by the glial cells, which protect neurons and induce an inflammatory response if the brain is injured. But this response also can contribute to seizures, some experts believe, either because components of the immune system stimulate neurons or because the glial cells' capacity to regulate the brain is diminished when they become "distracted" by an injury. As Dr. Devinsky noted, seizures in turn may produce further inflammation, perpetuating the cycle.

Now Dr. Vezzani and colleagues are testing a molecule called VX-765 that disrupts the inflammatory process she discovered. In one study, high doses of the drug reduced the number of seizures by about two-thirds in mice with treatment-resistant epilepsy.

Sixty patients enrolled in a subsequent trial did not experience a statistically significant improvement after taking VX-765 for six weeks, but they did begin to experience fewer seizures at the end of the trial.

The drug is now the subject of a Phase 2 trial involving 400 patients. "Anti-inflammatory therapies could at least supplement, and perhaps replace, anticonvulsants," said Dr. Jacqueline French, a neurologist at the N.Y.U. Comprehensive Epilepsy Center who is leading the new trial.

Replacing anticonvulsants is not merely an end in itself. Although they give many epileptics a better quality of life, they do not affect the course of the disease, only its symptoms. Researchers hope that anti-inflammatories may help ameliorate epilepsy's underlying causes. "Giving a medication that could treat the epilepsy, as opposed to treating the seizure, would be absolutely novel," Dr. French said.

But there are dangers to this approach. Steroids — potent anti-inflammatories that some doctors are using for experimental treatments — can have harmful long-term side effects. And it remains unclear whether inflammation might be implicated in all forms of epilepsy or which patients might benefit from anti-inflammatory treatment.

"Like any new field, there's a lot of enthusiasm and almost a bit of religion involved," said Dr. Tallie Z. Baram, an epilepsy expert at the University of California, Irvine. "The challenge for the next few years is to find out the limitations, the boundaries, the real mechanisms."

Still, whatever the role of inflammation in epilepsy, Elisa Moller says that anti-inflammatories were a miracle intervention for her son. At William's worst point, a night in July 2010, he had a seizure every time he fell asleep, suffering 23 grand mals between midnight and 6 a.m.

Dr. Devinsky had prescribed weekly injections of prednisone, a steroid, and in desperation Ms. Moller decided to administer a mega dose. "I was taking his life into my hands, I know," she said. "But the way I looked at it, he was going to die anyway."

Since that night William has not had another seizure. He continues with the steroids and also follows the ketogenic diet, a high-fat, low-carbohydrate regimen that has proved beneficial for many with intractable epilepsy.

Steroids are "the one thing I refuse to take him off of," Ms. Moller said. "The past year has been the best time of his life."

<http://nyti.ms/LITk8t>

**Zinc: Supplements for Babies Being Treated With Antibiotics Appear to Save Lives**  
***Giving zinc to newborns being treated with antibiotics for serious infections appears to save lives, according to a new study done in India.***

By DONALD G. McNEIL Jr.

The study, published online in The Lancet last week, compared more than 700 infants under 4 months old who had pneumonia, meningitis or sepsis; half got zinc and half got placebo. The zinc group had 40 percent less "treatment failure," by which the authors meant anything from death to a decision to switch antibiotics because standard ones were not working. Seventeen children in the placebo group died; only 10 who got zinc did. The study is "a major finding" but should be replicated before global policy is changed, said Dr. Robert E. Black, an expert in zinc supplementation at the Johns Hopkins Bloomberg School of Public Health who was not involved in the study.

Why zinc seems to help cure infections, diarrhea and pneumonia in zinc-deficient children is unknown, Dr. Black said. Zinc may work very differently when given briefly to dangerously ill children rather than as a supplement given regularly to healthy ones.

Vegetarian diets, like those of Hindus, are often zinc-deficient, Dr. Black said, but so are those of many malnourished children. Breast milk - even from zinc-deficient mothers - contains zinc, though it depletes the mother's reserves. But when rice or wheat gruel is added to a baby's diet, he said, phytates in the grain may block zinc absorption.

[http://www.eurekalert.org/pub\\_releases/2012-06/w-wad060112.php](http://www.eurekalert.org/pub_releases/2012-06/w-wad060112.php)

**We are drinking too much water**

***Our bodies need about two litres of fluids per day, not two litres of water specifically.***

In an Editorial in the June issue of Australian and New Zealand Journal of Public Health, Spero Tsindos from La Trobe University, examined why we consume so much water.

Mr Tsindos believes that encouraging people to drink more water is driven by vested interests, rather than a need for better health. "Thirty years ago you didn't see a plastic water bottle anywhere, now they appear as fashion accessories."

"As tokens of instant gratification and symbolism, the very bottle itself is seen as cool and hip," said Mr Tsindos. He also discusses the role of water in our constant quest for weight loss. "Drinking large amounts of water does not alone cause weight loss. A low-calorie diet is also required."

"Research has also revealed that water in food eaten has a greater benefit in weight reduction than avoiding foods altogether. We should be telling people that beverages like tea and coffee contribute to a person's fluid needs and despite their caffeine content, do not lead to dehydration."

"We need to maintain fluid balance and should drink water, but also consider fluid in unprocessed fruits and vegetables and juices."

[http://www.eurekalert.org/pub\\_releases/2012-06/plos-wci053112.php](http://www.eurekalert.org/pub_releases/2012-06/plos-wci053112.php)

**Waist circumference linked to diabetes risk, independently of body mass index**

***A collaborative re-analysis of data from the InterAct case-control study has established that waist circumference is associated with risk of type 2 diabetes, independently of body mass index.***

A collaborative re-analysis of data from the InterAct case-control study conducted by Claudia Langenberg and colleagues has established that waist circumference is associated with risk of type 2 diabetes, independently of body mass index (BMI). Reporting in this week's PLoS Medicine, the researchers estimated the association of BMI and waist circumference with type 2 diabetes from measurements of weight, height and waist circumference, finding that both BMI and waist circumference were independently associated with type 2 diabetes risk but waist circumference was a stronger risk factor in women than in men.

These findings indicate that targeted measurement of waist circumference in overweight individuals (who now account for a third of the US and UK adult population) could be an effective strategy for the prevention of diabetes because it would allow the identification of a high-risk subgroup of people who might benefit from individualised lifestyle advice. The authors comment: "Our results clearly show the value that measurement of [waist circumference] may have in identifying which people among the large population of overweight individuals are at highest risk of diabetes."

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Research Fund (FIS) of the Spanish Ministry of Health; the CIBER en Epidemiología y Salud Pública (CIBERESP), Spain, Murcia Regional Government (Nu 6236); JWJB, HBBdM, IS, AMWS, DLvdA, YTvdS: Dutch Ministry of Public Health, Welfare and Sports (VWS), Netherlands Cancer Registry (NKR), LK Research Funds, Dutch Prevention Funds, Dutch ZON (Zorg Onderzoek Nederland), World Cancer Research Fund (WCRF), Statistics Netherlands; verification of diabetes cases was additionally funded by NL Agency grant IGE05012 and an Incentive Grant from the Board of the UMC Utrecht; FLC: Cancer Research UK; PWF: Swedish Research Council, Novo Nordisk, Swedish Diabetes Association, Swedish Heart-Lung Foundation; GH: The county of Västerbotten; RK: German Cancer Aid, Federal Ministry of Education and Research; TJK: Cancer Research UK; KK: Medical Research Council UK, Cancer Research UK; PN: Swedish Research Council; JRQ: Asturias Regional Government; BT: German Cancer Aid; Federal Ministry of Education and Research; AT: Danish Cancer Society; RT: AIRE-ONLUS Ragusa, AVIS-Ragusa, Sicilian Regional Government.

Competing Interests: The authors have declared that no competing interests exist.

Citation: **The InterAct Consortium (2012) Long-Term Risk of Incident Type 2 Diabetes and Measures of Overall and Regional Obesity: The EPIC-InterAct Case-Cohort Study.** *PLoS Med* 9(6): e1001230. doi:10.1371/journal.pmed.1001230

[http://www.eurekalert.org/pub\\_releases/2012-06/cp-mid060112.php](http://www.eurekalert.org/pub_releases/2012-06/cp-mid060112.php)

### **Milk ingredient does a waistline good**

#### ***A natural ingredient found in milk can protect against obesity even as mice continue to enjoy diets that are high in fat.***

The researchers who report their findings in the June Cell Metabolism, a Cell Press publication, liken this milk ingredient to a new kind of vitamin. "This is present in what we've all been eating since day one," says Johan Auwerx of École Polytechnique Fédérale de Lausanne.

The researchers identified this ingredient, known as nicotinamide riboside, as they were searching for alternative ways to boost the well-known gene SIRT1, which comes with benefits for both metabolism and longevity. One way to do that is to target SIRT1 directly, as the red wine ingredient resveratrol appears to do, at least at some doses.

Auwerx's team suspected there might be a simpler way to go about it, by boosting levels of one of SIRT1's molecular sidekicks, the cofactor NAD<sup>+</sup>. This milk ingredient does just that in a rather appealing way. Not only is it a natural product, but it also gets trapped within cells, where it can do its magic.

Mice that take nicotinamide riboside in fairly high doses along with their high-fat meals burn more fat and are protected from obesity. They also become better runners thanks to muscles that have greater endurance. The benefits they observe in mice wouldn't be easy to get from drinking milk alone, Auwerx says. It may be more likely that the compound would serve as a new kind of metabolism-boosting supplement. Tests done in people are now needed to help sort out those details.

On the other hand, he says, this milk substance ultimately offers the same benefits attributed to resveratrol, but in a different way. It's possible that many small effects of ingredients found in our diets could add up to slimmer waistlines—perhaps longer lives, too.

*Canto et al.: "The NAD<sup>+</sup> precursor nicotinamide riboside enhances oxidative metabolism and protects against high-fat diet induced obesity."*

[http://www.eurekalert.org/pub\\_releases/2012-06/jaaj-sem053112.php](http://www.eurekalert.org/pub_releases/2012-06/jaaj-sem053112.php)

### **Study examines major bleeding risk with low-dose aspirin use in patients with and without diabetes**

#### ***Among nearly 200,000 individuals, daily use of low-dose aspirin was associated with an increased risk of major gastrointestinal or cerebral bleeding, according to a study in the June 6 issue of JAMA.***

CHICAGO – The authors also found that patients with diabetes had a high rate of major bleeding, irrespective of aspirin use.

"Therapy with low-dose aspirin is used for the treatment of cardiovascular disease. It is recommended as a secondary prevention measure for individuals with moderate to high risk of cardiovascular events (i.e., for patients with multiple risk factors such as hypertension, dyslipidemia, obesity, diabetes, and family history of ischemic heart disease)," according to background information in the article. "Any benefit of low-dose aspirin might be offset by the risk of major bleeding. It is known that aspirin is associated with gastrointestinal and intracranial hemorrhagic complications. However, randomized controlled trials have shown that these risks are relatively small."

The authors add that randomized controlled trials evaluate selected patient groups and do not necessarily generalize to an entire population.

In addition, low-dose aspirin use is recommended for certain patients with diabetes. Findings from a meta-analysis suggested that diabetes may increase the risk of extracranial hemorrhage. "These estimates were

derived from a limited number of events within randomized trials. Hence, the risk-to-benefit ratio for the use of low-dose aspirin in the presence of diabetes mellitus remains to be clarified," the researchers write.

Giorgia De Berardis, M.Sc., of Consorzio Mario Negri Sud, Santa Maria Imbaro, Italy, and colleagues conducted a study to determine the incidence of major gastrointestinal and intracranial bleeding episodes in individuals with and without diabetes taking aspirin.

For the study, the researchers used administrative data from 4.1 million citizens in 12 local health authorities in Puglia, Italy. Individuals with new prescriptions for low-dose aspirin (300 mg or less) were identified during the index period from January 2003 to December 2008, and were matched with individuals who did not take aspirin during this period.

For the study, the researchers included 186,425 individuals being treated with low-dose aspirin and 186,425 matched controls without aspirin use. During 6 years, 6,907 first episodes of major bleeding requiring hospitalization were registered, of which there were 4,487 episodes of gastrointestinal bleeding and 2,464 episodes of intracranial hemorrhage.

Analysis indicated that the use of aspirin was associated with a 55 percent increased relative risk of gastrointestinal bleeding and 54 percent increased relative risk of intracranial bleeding. The authors note that in comparison with other estimates of rates of major bleeding, their findings indicate a 5-times higher incidence of major bleeding leading to hospitalization among both aspirin users and those without aspirin use.

Regarding the use of aspirin being associated with a 55 percent relative risk increase in major bleeding, "this translates to 2 excess cases for 1,000 patients treated per year. In other words, the excess number of major bleeding events associated with the use of aspirin is of the same magnitude of the number of major cardiovascular events avoided in the primary prevention setting for individuals with a 10-year risk of between 10 percent and 20 percent," they write.

The researchers also found that the use of aspirin was associated with a greater risk of major bleeding in most of the subgroups evaluated, but not in individuals with diabetes. Diabetes was independently associated with a 36 percent increased relative risk of major bleeding episodes, irrespective of aspirin use. Among individuals not taking aspirin, those with diabetes had an increased relative risks of 59 percent for gastrointestinal bleeding and 64 percent for intracranial bleeding.

"Our study shows, for the first time, to our knowledge, that aspirin therapy only marginally increases the risk of bleeding in individuals with diabetes," the authors write. "These results can represent indirect evidence that the efficacy of aspirin in suppressing platelet function is reduced in this population."

"In conclusion, weighing the benefits of aspirin therapy against the potential harms is of particular relevance in the primary prevention setting, in which benefits seem to be lower than expected based on results in high-risk populations. In this population-based cohort, aspirin use was significantly associated with an increased risk of major bleeding, but this association was not observed for patients with diabetes. In this respect, diabetes might represent a different population in terms of both expected benefits and risks associated with antiplatelet therapy."

*(JAMA. 2012;307[21]:2286-2294. Available pre-embargo to the media at <http://media.jamanetwork.com>)*

*Editor's Note: Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.*

### ***Editorial: Hemorrhagic Complications Associated With Aspirin - An Underestimated Hazard in Clinical Practice?***

In an accompanying editorial, Jolanta M. Siller-Matula, M.D., Ph.D., of the Medical University of Vienna, Austria, comments on the findings of this study, and writes that "a decision-making process based on balancing an individual patient's risk of bleeding and ischemic events is difficult."

"The study by De Berardis et al underscores that the potential risk of bleeding should be carefully considered in decision making. Assessment of bleeding risk and of net clinical benefit will merit further emphasis as issues inherent to aspirin use also apply to more potent platelet inhibitors and anticoagulants; there is only a thin line between efficacy and safety, and the reduction in ischemic events comes at the cost of increased major bleedings. Therefore, future studies investigating the risks and benefits for individual patients appear to be mandatory to help physicians appropriately make recommendations about aspirin use for primary prevention."

*(JAMA. 2012;307[21]:2318-2320. Available pre-embargo to the media at <http://media.jamanetwork.com>)*

*Editor's Note: The author completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr. Siller-Matula reported receiving speaker fees from Eli Lilly and AstraZeneca.*

## **Dinosaurs lighter than previously thought**

***Scientists have developed a new technique to accurately measure the weight and size of dinosaurs and discovered they are not as heavy as previously thought.***

University of Manchester biologists used lasers to measure the minimum amount of skin required to wrap around the skeletons of modern-day mammals, including reindeer, polar bears, giraffes and elephants. They discovered that the animals had almost exactly 21% more body mass than the minimum skeletal 'skin and bone' wrap volume, and applied this to a giant Brachiosaur skeleton in Berlin's Museum für Naturkunde. Previous estimates of this Brachiosaur's weight have varied, with estimates as high as 80 tonnes, but the Manchester team's calculations – published in the journal *Biology Letters* – reduced that figure to just 23 tonnes. The team says the new technique will apply to all dinosaur weight measurements.

Lead author Dr Bill Sellers said: "One of the most important things palaeobiologists need to know about fossilised animals is how much they weighed. This is surprisingly difficult, so we have been testing a new approach. We laser scanned various large mammal skeletons, including polar bear, giraffe and elephant, and calculated the minimum wrapping volume of the main skeletal sections. "We showed that the actual volume is reliably 21% more than this value, so we then laser scanned the Berlin Brachiosaur, *Giraffatitan brancai*, calculating the skin and bone wrapping volume and added 21%. We found that the giant herbivore weighed 23 tonnes, supporting the view that these animals were much lighter than traditionally thought.

Dr Sellers, based in Manchester's Faculty of Life Sciences, explained that body mass was a critical parameter used to constrain biomechanical and physiological traits of organisms. He said: "Volumetric methods are becoming more common as techniques for estimating the body masses of fossil vertebrates but they are often accused of excessive subjective input when estimating the thickness of missing soft tissue.

"Here, we demonstrate an alternative approach where a minimum convex hull is derived mathematically from the point cloud generated by laser-scanning mounted skeletons. This has the advantage of requiring minimal user intervention and is therefore more objective and far quicker.

"We tested this method on 14 large-bodied mammalian skeletons and demonstrated that it consistently underestimated body mass by 21%. We suggest that this is a robust method of estimating body mass where a mounted skeletal reconstruction is available and demonstrate its usage to predict the body mass of one of the largest, relatively complete sauropod dinosaurs, *Giraffatitan brancai*, as 23,200 kg.

"The value we got for *Giraffatitan* is at the low range of previous estimates; although it is still huge, some of the enormous estimates of the past – 80 tonnes in 1962 – are exaggerated. Our method provides a much more accurate measure and shows dinosaurs, while still huge, are not as big as previously thought."

<http://arstechnica.com/science/2012/06/adding-iron-is-like-giving-early-rna-enzymes-steroids/>

## **Adding iron is like giving early RNA enzymes "steroids"**

***The RNA world that came before life might have gotten a big boost from iron.***

**by Melissa Fellet - June 5 2012, 10:23pm TST**

Life may have started from an RNA world, where RNA both carried genetic information and catalyzed chemical reactions, jobs that are now divided between DNA and proteins. But sussing out the chemistry of the RNA world is challenging, not least because we'll never really know what metals and molecules were present on the early Earth. Scientists have some clues from the chemistry of rocks, computer models, and lab experiments.



***Iron, trapped in this rock as bands of rust, would have been dissolved in watery pools on early Earth. flickr.com***

New research suggests that RNA on the early Earth could have interacted with different metals than it does today. Magnesium currently helps our RNA fold into the proper shapes for catalysis. Changing that metal to iron could increase the types of reactions that could be catalyzed by early RNAs.

Iron dissolved in watery pools was plentiful on the oxygen-free early Earth. Once photosynthetic organisms appeared and started pumping out oxygen, that iron turned to rust, and was trapped in rocks as bands still visible today. Since the RNA world is thought to have existed before this Great Oxidation Event, Loren Williams at Georgia Institute of Technology and his colleagues wondered if RNA on early Earth could have bound iron.

First, the researchers modeled a snippet of the RNA backbone – just one sugar flanked by two phosphate groups. They plunked a magnesium or an iron ion in between the phosphates and calculated the most stable shape of the backbone. Both backbones had the same shape, regardless of metal ion inside.

Knowing that an iron ion (Fe<sup>2+</sup>) could fit in the same place as Mg<sup>2+</sup> in RNA, the researchers tested modern RNA enzymes, or ribozymes, to see if they would still function with iron under oxygen-free conditions. One ribozyme, a ligase that connects RNA molecules, was actually 25 times more active using iron than magnesium. The other ribozyme snipped RNA apart three times faster when it bound iron instead of magnesium. Not only can modern RNA enzymes bind iron, they also work more efficiently using that ion. What else might iron do for the function of early ribozymes? Iron can transfer electrons more efficiently than magnesium. Ancient ribozymes holding iron could likely perform a broader range of reactions than modern ones, since they could shuffle electrons between molecules more efficiently. (Most of basic metabolism, like conversion of sugars into usable energy, involves electron transfer reactions.)

An RNA world with iron would be the RNA world on steroids, the researchers write. Over time, less-reactive magnesium ions may have replaced the iron ions because they better stabilize folded RNAs.

The researchers plan to continue to study the chemistry of iron-RNA complexes, looking for reactions not possible with magnesium.

Making molecules that resemble ones we find in life today is simple. Stanley Miller did it in 1953, when he combined ammonia, hydrogen, methane and water vapor in a jar and zapped the mixture with a lightning bolt. In that primordial soup, Miller found building blocks of proteins and simpler molecules like urea that could be used to build more complicated biochemicals. Analyzing that mixture more than 50 years later with modern methods, researchers found even more amino acids than Miller originally thought.

Now, many researchers are looking into how collections of these simple molecules started interacting. "The big challenge today is figuring how you select, concentrate, and assemble all of those molecules into a larger lifelike system, one which starts to make copies of itself," geophysicist Robert Hazen of the Carnegie Institution of Washington told the Economist this week. "And that remains a huge mystery."

Catalysts, whether salts, metals or nucleic acids, can help with the selection process. They guide chemical reactions away from a sticky mix of products to a group of specific molecules. So identifying early catalysts could help scientists identify possible chemical reactions that could lead to the building blocks of life.

PLoS ONE, 2012. DOI: 10.1371/journal.pone.0038024 (About DOIs).

[http://www.eurekalert.org/pub\\_releases/2012-06/f-sf-hhw060612.php](http://www.eurekalert.org/pub_releases/2012-06/f-sf-hhw060612.php)

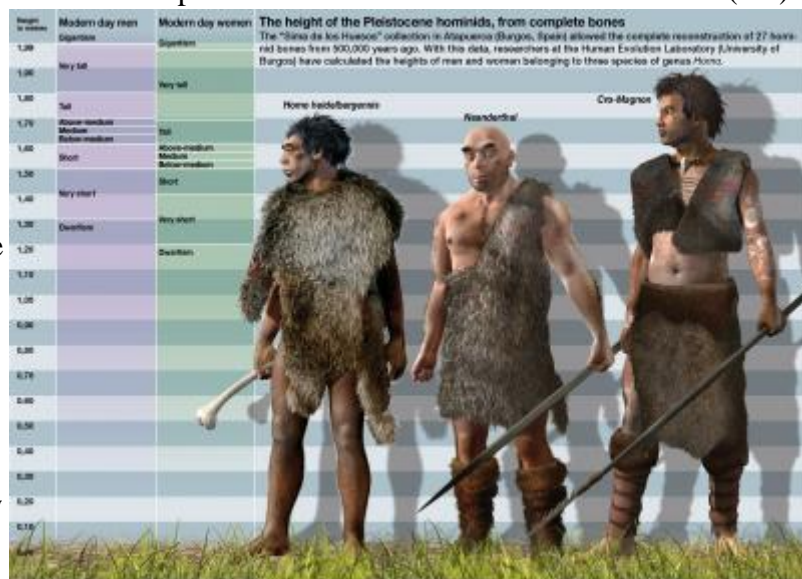
### Homo heidelbergensis was only slightly taller than the Neanderthal

#### **Reconstruction of human limb bones has helped to determine the height of Pleistocene era species. Homo heidelbergensis were similar in height to the current Mediterranean population.**

The reconstruction of 27 complete human limb bones found in Atapuerca (Burgos, Spain) has helped to determine the height of various species of the Pleistocene era. Homo heidelbergensis, like Neanderthals, were similar in height to the current population of the Mediterranean.

Along with its enormous quantity of fossils, one of the most important features of the Sima de los Huesos (SH) site in Atapuerca, Burgos, is the splendid state of the findings. They are so well conserved that the 27 complete bones from some 500,000 years ago have been reconstructed.

"The incredible collection allows us to estimate the height of species such as Homo heidelbergensis, who inhabited Europe during the Middle Pleistocene era and is the ancestor of the Neanderthal. Such estimations are based solely on analysis of the large complete bones, like those from the arm and the leg," as explained to SINC by José Miguel Carretero Díaz, researcher at the Laboratory of Human Evolution of the University of Burgos and lead author of the study that has been published in the 'Journal of Human Evolution' journal.



**This image shows the height of the Pleistocene hominids, from complete bones. Credit: SINC / José Antonio Peñas**

In addition, since bones were complete, the researchers were able to determine whether they belonged to a male or female and thus calculate the height of both men and women. "Estimations to date were based on incomplete bone samples, the length of which had to be estimated too. We also used to use formulas based on just one reference population and we were not even sure as to its appropriateness," outlines the researcher.

Since the most fitting race or ecology for these human beings was unknown, scientists used multiracial and multigender formulas to estimate the height for the entire population in order to reduce the error margin and get a closer insight on the reality. As Carretero Díaz points out, "we calculated an overall average for the sample and one for each of the sexes. The same was done with the Neanderthal and Cro-Magnon fossils."

The results suggest that both men and women in the Sima de los Huesos population were on average slightly higher than Neanderthal men and women. "Neither can be described as being short and both are placed in the medium and above-medium height categories. But, both species featured tall individuals," assured the experts. The height of these two species is similar to that of modern day population of mid-latitudes, like in the case of Central Europe and the Mediterranean.

The humans who arrived in Europe during the Upper Palaeolithic era, Cro-Magnons or anatomically modern humans, replaced the Neanderthal populations. They were significantly taller than other human species and their average height for both sexes was higher, falling in the very tall individual category.

### Height remained the same for some 2 million years

According to the researchers, putting aside the margin corresponding to small biotype species like *Homo habilis* (East Africa), *Homo georgicus* (Georgia) and *Homo floresiensis* (Flores in Indonesia), all documented humans during the Early and Middle Pleistocene Era that inhabited Africa (*Homo ergaster*, *Homo rhodesiensis*), Asia (*Homo erectus*) and Europe (*Homo antecessor*, *Homo heidelbergensis* and *Homo neanderthalensis*) seemed to have medium and above-medium heights for the most part of two millions years. However, the researchers state that "amongst every population we have found a tall or very tall individual."

In their opinion, this suggests that the height of the *Homo* genus remained more or less stable for 2 million years until the appearance of a "ground-breaking species in this sense" in Africa just 200,000 years ago. These were the *Homo sapiens*, who were initially significantly taller than any other species that existed at the time. "The explanation is found in the overall morphological change in the body biotype that prevailed in our species compared to our ancestors. The *Homo sapiens* had a slimmer body, lighter bones, longer legs and were taller," adds the researcher.

### A lighter body aided survival

Scientists have documented various advantages that made the *sapiens* biotype more adaptable. These include their thermoregulatory, obstetric and nutritional make-up but in the eyes of the experts, the greatest advantage of this new body type was increased endurance and energy.

Carretero Díaz indicates that "larger legs, narrower hips, being taller and having lighter bones not only meant a reduction in body weight (less muscular fat) but a bigger stride, greater speed and a lower energy cost when moving the body, walking or running."

This type of anatomy could have been highly advantageous in terms of survival in Eurasia during the Upper Pleistocene Era when two intelligent human species (the light-bodied Cro-Magnons and Neanderthals) had to face difficult climatic conditions, drastic changes in ecosystems and ecological competition.

Carretero et al., "Estimación de la estatura en los humanos del yacimiento de la Sima de los Huesos (Sierra de Atapuerca, Burgos) basada en huesos largos completos" *Journal of Human Evolution* 62: 242-255, 2012.  
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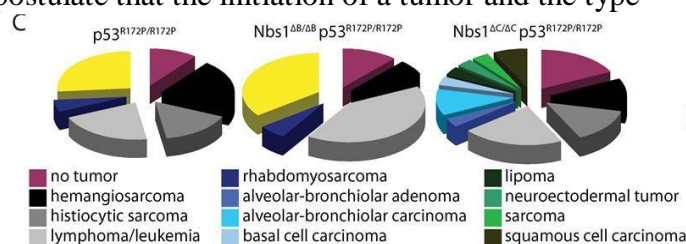
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## New Clues About the Origin of Cancer

### A study reveals new information about the origin of tumors.

ScienceDaily - A study by Travis H. Stracker, researcher at the Institute for Research in Biomedicine (IRB Barcelona), in collaboration with scientists at the Memorial Sloan Kettering Cancer Center (MSKCC) in New York, reveals new information about the origin of tumors. In this study, published in the journal *Proceedings of the National Academy of Sciences (PNAS)*, the scientists postulate that the initiation of a tumor and the type and aggressivity of the same depend on a specific

combination of defects in several processes that safeguard cell integrity, such as DNA repair pathways and cell cycle check-points. The study also demonstrates that mice with a high degree of chromosomal instability and defective programmed cell death (apoptosis), two hallmarks of cancer, rarely develop tumors.



*Different types of tumor arise, depending on the mutation of certain proteins involved in DNA damage response, cell cycle check-points and apoptosis. (Credit: Image courtesy of Institute for Research in Biomedicine-IRB)*

"Whether or not a tumor develops depends on the moment of the cell cycle in which the damage occurs, which repair pathways components are affected, and which others are impaired in terms of apoptosis and cell cycle arrest," explains the North-American Travis H. Stracker, head of the "Genomic Instability and Cancer" group and an expert in DNA repair pathways and its implications on human health. In this study, H. Stracker and his team report on some of these combinations for the initiation of cancer and in different kinds of tissue. "The paper points out that our understanding of which aspects of damage response promote tumorigenesis and where they play a role in the process needs to be investigated further because it shows that it has been generalized and that there is a lot of specifics that are not at all clear."

The researchers utilized mice carrying mutations in key DNA repair genes involved in cancer. Next, they combined them with other mutations affecting cell cycle checkpoints or apoptosis until they hit upon the combinations that are sufficient to initiate tumorigenesis or to generate certain types of tumors. "It is like deconstructing cancer to find the factors responsible for it appearing," says H. Stracker. During DNA replication in a dividing cell there is a series of checkpoints to test that duplication is taking place properly. If the cell detects errors in any of these phases, cell growth is halted and highly complex DNA repair processes are triggered. If the repair is defective and the cell accumulates many genomic errors, "watch-out" proteins step in, such as tumor suppressor p53. Such proteins activate programmed cell death (apoptosis) or cell cycle arrest (senescence). "A very complex network of pathways and proteins are involved," explains the researcher. "This study demonstrates that genomic instability per se is not sufficient to initiate a tumor and that we cannot generalize. We need to study the origin of different kinds of cancer in much greater depth and although it is as difficult as trying to find a needle in a haystack, we are slowly identifying the parts on which we should focus," he goes on to explain. The detection of the main players that cause different kinds of cancer could be of great interest for the design of new diagnostic tools and specific treatments.

S. S. Foster, S. De, L. K. Johnson, J. H. J. Petrini, T. H. Stracker. *Cell cycle- and DNA repair pathway-specific effects of apoptosis on tumor suppression. Proceedings of the National Academy of Sciences, 2012; DOI: 10.1073/pnas.1120476109*

<http://www.sciencedaily.com/releases/2012/06/120606102710.htm>

### **Complex World of Gut Microbes Fine-Tune Body Weight**

***Recently, researchers have begun to untangle the subtle role these diverse life forms play in maintaining health and regulating weight.***

ScienceDaily - Microorganisms in the human gastrointestinal tract form an intricate, living fabric made up of some 500 to 1000 distinct bacterial species, (in addition to other microbes). Recently, researchers have begun to untangle the subtle role these diverse life forms play in maintaining health and regulating weight.

In a new study appearing in the journal *Nutrition in Clinical Practice*, researcher Rosa Krajmalnik-Brown and her colleagues at the Swette Center for Environmental Biotechnology at Arizona State University's Biodesign Institute in collaboration with John DiBaise from the Division of Gastroenterology at the Mayo Clinic, review the role of gut microbes in nutrient absorption and energy regulation.

According to Krajmalnik-Brown, "Malnutrition may manifest as either obesity or undernutrition, problems of epidemic proportion worldwide. Microorganisms have been shown to play an important role in nutrient and energy extraction and energy regulation although the specific roles that individual and groups/teams of gut microbes play remain uncertain."

The study outlines the growth of varied microbial populations -- from birth onwards -- highlighting their role in extracting energy from the diet. The composition of microbial communities is shown to vary with age, body weight, and variety of food ingested; as well as in response to bariatric surgery for obesity, use of antibiotics and many other factors.

Based on current findings, the authors suggest that therapeutic modification of the gut microbiome may offer an attractive approach to future treatment of nutrition-related maladies, including obesity and a range of serious health consequences linked to under-nutrition.

#### **Micromanagers**

The microbes in the human gut belong to three broad domains, defined by their molecular phylogeny: Eukarya, Bacteria, and Achaea. Of these, bacteria reign supreme, with two dominant divisions -- known as Bacteroidetes and Firmicutes -- making up over 90 percent of the gut's microbial population. In contrast, the Achaea that exist in the gut are mostly composed of methanogens (producers of methane) and specifically by *Methanobrevibacter smithii* -- a hydrogen-consumer.

Within the bacterial categories however, enormous diversity exists. Each individual's community of gut microbes is unique and profoundly sensitive to environmental conditions, beginning at birth. Indeed, the mode of delivery during the birthing process has been shown to affect an infant's microbial profile.



Communities of vaginal microbes change during pregnancy in preparation for birth, delivering beneficial microbes to the newborn. At the time of delivery, the vagina is dominated by a pair of bacterial species, *Lactobacillus* and *Prevotella*. In contrast, infants delivered by caesarean section typically show microbial communities associated with the skin, including *Staphylococcus*, *Corynebacterium*, and *Propionibacterium*. While the full implications of these distinctions are still murky, evidence suggests they may affect an infant's subsequent development and health, particularly in terms of susceptibility to pathogens.

### **Diet and destiny**

After birth, diet becomes a critical determinant in microbial diversity within the gut. Recent research indicates that microbial populations vary geographically in a manner consistent with regional differences in diet. Children in rural areas of Burkina Faso for example showed much more abundant concentrations of *Bacteroidetes* compared with their cohorts in Italy, a finding consistent with the African children's plant-rich diet.

While microbiomes appear to have adapted to local diets, changes in eating habits significantly alter composition of gut microbes. Variations in macronutrient composition can modify the structure of gut microbiota in a few days -- in some cases, a single day. Studies in mice show that changing from a low fat, plant polysaccharide diet to a Western diet high in sugar and fat rapidly and profoundly reconfigures the composition of microbes in the gut.

Another modifier of gut microbe composition is gastric bypass surgery, used in certain cases to alleviate conditions of serious obesity. In earlier work, the authors found that the post-surgical microbial composition of patients who underwent so-called Roux-en-Y gastric bypass was distinct from both obese and normal weight individuals.

"Obesity affects more than a third of adults in the U.S. and is associated with a raft of health conditions including heart disease, stroke, type 2 diabetes and certain forms of cancer," says Dr. John DiBaise. The authors further note that concentrations in the blood of lipopolysaccharides derived from gut bacteria increase in obese individuals, producing a condition known as metabolic endotoxemia. The disorder has been linked with chronic, systemic, low-level inflammation as well as insulin resistance.

### **Energy harvest**

In the current review, the cycle of microbial energy extraction from food, involving hydrogen-producing and consuming reactions in the human intestine, is described in detail. Short chain fatty acids (SCFAs) are a critical component in this system. During the digestive process, fermentation in the gut breaks down complex organic compounds, producing SCFA and hydrogen. The hydrogen is either excreted in breath or consumed by 3 groups of microorganisms inhabiting the colon: methanogens, acetogens and sulfate reducers.

Research conducted by the authors and others has demonstrated that hydrogen-consuming methanogens appear in greater abundance in obese as opposed to normal weight individuals. Further, the Firmicutes -- a form of acetogen -- also seem to be linked with obesity. Following fermentation, SCFAs persist in the colon. Greater concentration of SCFAs, especially propionate, were observed in fecal samples from obese as opposed to normal weight children. (SCFAs also behave as signaling molecules, triggering the expression of leptin, which acts as an appetite suppressor.)

While it now seems clear that certain microbial populations help the body process otherwise indigestible carbohydrates and proteins, leading to greater energy extraction and associated weight gain, experimental results have shown some inconsistency. For example, while a number of studies have indicated a greater prevalence of *Bacteroidetes* in lean individuals and have linked the prevalence of Firmicutes with obesity, the authors stress that many questions remain.

Alterations in gut microbiota are also of crucial concern for the one billion people worldwide who suffer from undernutrition. Illnesses resulting from undernutrition contribute to over half of the global fatalities in children under age 5. Those who do survive undernutrition often experience a range of serious, long-term mental and physical effects. The role of gut microbial diversity among the undernourished has yet to receive the kind of concentrated research effort applied to obesity -- a disease which has reached epidemic proportions in the developed world.

Exploiting microbes affecting energy extraction may prove a useful tool for non-surgically addressing obesity as well as treating undernutrition, though more research is needed for a full understanding of regulatory mechanisms governing the delicate interplay between intestinal microbes and their human hosts.

Dr. Krajmalnik-Brown and colleagues at the Biodesign Institute and Mayo Clinic are currently in the second year of an NIH-funded study to better understand the role of the gut microbiome in the success or failure of

surgical procedures performed to treat obesity including the Roux-en-Y gastric bypass, adjustable gastric band and vertical sleeve gastrectomy.

R. Krajmalnik-Brown, Z.-E. Ilhan, D.-W. Kang, J. K. DiBaise. *Effects of Gut Microbes on Nutrient Absorption and Energy Regulation. Nutrition in Clinical Practice, 2012; 27 (2): 201 DOI: 10.1177/0884533611436116*

<http://www.sciencedaily.com/releases/2012/06/120606111801.htm>

## **Statistical Model Attempting to Estimate Level of Alcohol Consumption That Is 'Optimal' for Health**

***Half a unit of alcohol is as little as a quarter of a glass of wine, or a quarter of a pint.***

ScienceDaily - Cutting the amount we drink to just over half a unit a day could save 4,600 lives a year in England, according to a modelling study by Oxford University researchers published in the journal *BMJ Open*.

Scientists have carried out a complex analysis in an attempt to determine the "optimal" level of alcohol consumption that is associated with the lowest rates of chronic disease in the UK.

They conclude that the intake of about one-half of a typical drink per day would result in the healthiest outcomes, and the authors conclude that the recommended alcohol intake for the UK should be reduced from the current advised level of drinking.

Half a unit of alcohol is as little as a quarter of a glass of wine, or a quarter of a pint. That's much lower than current government recommendations of between 3 to 4 units a day for men and 2-3 units for women.

The researchers set out to find the optimum daily amount of alcohol that would see fewest deaths across England from a whole range of diseases connected to drink. Previous studies have often looked at the separate effects of alcohol on heart disease, liver disease or cancers in isolation.

'Although there is good evidence that moderate alcohol consumption protects against heart disease, when all of the chronic disease risks are balanced against each other, the optimal consumption level is much lower than many people believe,' says lead author Dr Melanie Nichols of the BHF Health Promotion Research Group in the Department of Public Health at Oxford University.

The team used a mathematical model to assess what impact changing average alcohol consumption would have on deaths from 11 conditions known to be at least partially linked to drink.

These included coronary heart disease, stroke, high blood pressure, diabetes, cirrhosis of the liver, epilepsy, and five cancers. Over 170,000 people in England died from these 11 conditions in 2006, and ill health linked to alcohol is estimated to cost the NHS in England £3.3 billion every year.

The researchers used information from the 2006 General Household Survey on levels of alcohol consumption among adults in England. They combined this with the disease risks for differing levels of alcohol consumption as established in large analyses of published research.

They found that just over half a unit of alcohol a day was the optimal level of consumption among current drinkers.

They calculate this level of drinking would prevent around 4,579 premature deaths, or around 3% of all deaths from the 11 conditions.

The number of deaths from heart disease would increase by 843, but this would be more than offset by around 2,600 fewer cancer deaths and almost 3,000 fewer liver cirrhosis deaths.

'Moderating your alcohol consumption overall, and avoiding heavy-drinking episodes, is one of several things, alongside a healthy diet and regular physical activity, that you can do to reduce your risk of dying early of chronic diseases,' says Dr Nichols.

She adds: 'We are not telling people what to do, we are just giving them the best balanced information about the different health effects of alcohol consumption, so that they can make an informed decision about how much to drink.'

'People who justify their drinking with the idea that it is good for heart disease should also consider how alcohol is increasing their risk of other chronic diseases. A couple of pints or a couple of glasses of wine per day is not a healthy option.'

Although this study in *BMJ Open* did not look at patterns of drinking, Dr Nichols says: 'Regardless of your average intake, if you want to have the best possible health, it is also very important to avoid episodes of heavy drinking ("binge drinking") as there is very clear evidence that this will increase your risks of many diseases, as well as your risk of injuries.'

M. Nichols, P. Scarborough, S. Allender, M. Rayner. *What is the optimal level of population alcohol consumption for chronic disease prevention in England? Modelling the impact of changes in average consumption levels. BMJ Open, 2012; 2 (3): e000957 DOI: 10.1136/bmjopen-2012-000957*

## **Evidence of Impending Tipping Point for Earth**

### ***The Earth may be approaching a tipping point due to climate change and increasing population.***

ScienceDaily - A group of scientists from around the world is warning that population growth, widespread destruction of natural ecosystems, and climate change may be driving Earth toward an irreversible change in the biosphere, a planet-wide tipping point that would have destructive consequences absent adequate preparation and mitigation.

"It really will be a new world, biologically, at that point," warns Anthony Barnosky, professor of integrative biology at the University of California, Berkeley, and lead author of a review paper appearing in the June 7 issue of the journal *Nature*. "The data suggests that there will be a reduction in biodiversity and severe impacts on much of what we depend on to sustain our quality of life, including, for example, fisheries, agriculture, forest products and clean water. This could happen within just a few generations."

The *Nature* paper, in which the scientists compare the biological impact of past incidents of global change with processes under way today and assess evidence for what the future holds, appears in an issue devoted to the environment in advance of the June 20-22 United Nations Rio+20 Earth Summit in Rio de Janeiro, Brazil. The result of such a major shift in the biosphere would be mixed, Barnosky noted, with some plant and animal species disappearing, new mixes of remaining species, and major disruptions in terms of which agricultural crops can grow where.

The paper by 22 internationally known scientists describes an urgent need for better predictive models that are based on a detailed understanding of how the biosphere reacted in the distant past to rapidly changing conditions, including climate and human population growth. In a related development, ground-breaking research to develop the reliable, detailed biological forecasts the paper is calling for is now underway at UC Berkeley. The endeavor, The Berkeley Initiative in Global Change Biology, or BiGCB, is a massive undertaking involving more than 100 UC Berkeley scientists from an extraordinary range of disciplines that already has received funding: a \$2.5 million grant from the Gordon and Betty Moore Foundation and a \$1.5 million grant from the Keck Foundation. The paper by Barnosky and others emerged from the first conference convened under the BiGCB's auspices.

"One key goal of the BiGCB is to understand how plants and animals responded to major shifts in the atmosphere, oceans, and climate in the past, so that scientists can improve their forecasts and policy makers can take the steps necessary to either mitigate or adapt to changes that may be inevitable," Barnosky said. "Better predictive models will lead to better decisions in terms of protecting the natural resources future generations will rely on for quality of life and prosperity." Climate change could also lead to global political instability, according to a U.S. Department of Defense study referred to in the *Nature* paper.

"UC Berkeley is uniquely positioned to conduct this sort of complex, multi-disciplinary research," said Graham Fleming, UC Berkeley's vice chancellor for research. "Our world-class museums hold a treasure trove of biological specimens dating back many millennia that tell the story of how our planet has reacted to climate change in the past. That, combined with new technologies and data mining methods used by our distinguished faculty in a broad array of disciplines, will help us decipher the clues to the puzzle of how the biosphere will change as the result of the continued expansion of human activity on our planet."

One BiGCB project launched last month, with UC Berkeley scientists drilling into Northern California's Clear Lake, one of the oldest lakes in the world with sediments dating back more than 120,000 years, to determine how past changes in California's climate impacted local plant and animal populations.

City of Berkeley Mayor Tom Bates, chair of the Bay Area Joint Policy Committee, said the BiGCB "is providing the type of research that policy makers urgently need as we work to reduce greenhouse gas emissions and prepare the Bay region to adapt to the inevitable impacts of climate change. To take meaningful actions to protect our region, we first need to understand the serious global and local changes that threaten our natural resources and biodiversity."

"The Bay Area's natural systems, which we often take for granted, are absolutely critical to the health and well-being of our people, our economy and the Bay Area's quality of life," added Bates.

### **How close is a global tipping point?**

The authors of the *Nature* review -- biologists, ecologists, complex-systems theoreticians, geologists and paleontologists from the United States, Canada, South America and Europe -- argue that, although many warning signs are emerging, no one knows how close Earth is to a global tipping point, or if it is inevitable. The scientists urge focused research to identify early warning signs of a global transition and an acceleration of efforts to address the root causes.

"We really do have to be thinking about these global scale tipping points, because even the parts of Earth we are not messing with directly could be prone to some very major changes," Barnosky said. "And the root cause, ultimately, is human population growth and how many resources each one of us uses."

Coauthor Elizabeth Hadly from Stanford University said "we may already be past these tipping points in particular regions of the world. I just returned from a trip to the high Himalayas in Nepal, where I witnessed families fighting each other with machetes for wood -- wood that they would burn to cook their food in one evening. In places where governments are lacking basic infrastructure, people fend for themselves, and biodiversity suffers. We desperately need global leadership for planet Earth."

The authors note that studies of small-scale ecosystems show that once 50-90 percent of an area has been altered, the entire ecosystem tips irreversibly into a state far different from the original, in terms of the mix of plant and animal species and their interactions. This situation typically is accompanied by species extinctions and a loss of biodiversity.

Currently, to support a population of 7 billion people, about 43 percent of Earth's land surface has been converted to agricultural or urban use, with roads cutting through much of the remainder. The population is expected to rise to 9 billion by 2045; at that rate, current trends suggest that half Earth's land surface will be disturbed by 2025. To Barnosky, this is disturbingly close to a global tipping point.

"Can it really happen? Looking into the past tells us unequivocally that, yes, it can really happen. It has happened. The last glacial/interglacial transition 11,700 years ago was an example of that," he said, noting that animal diversity still has not recovered from extinctions during that time. "I think that if we want to avoid the most unpleasant surprises, we want to stay away from that 50 percent mark."

### **Global change biology**

The paper emerged from a conference held at UC Berkeley in 2010 to discuss the idea of a global tipping point, and how to recognize and avoid it.

Following that meeting, 22 of the attendees summarized available evidence of past global state-shifts, the current state of threats to the global environment, and what happened after past tipping points.

They concluded that there is an urgent need for global cooperation to reduce world population growth and per-capita resource use, replace fossil fuels with sustainable sources, develop more efficient food production and distribution without taking over more land, and better manage the land and ocean areas not already dominated by humans as reservoirs of biodiversity and ecosystem services.

"Ideally, we want to be able to predict what could be detrimental biological change in time to steer the boat to where we don't get to those points," Barnosky said. "My underlying philosophy is that we want to keep Earth, our life support system, at least as healthy as it is today, in terms of supporting humanity, and forecast when we are going in directions that would reduce our quality of life so that we can avoid that."

"My view is that humanity is at a crossroads now, where we have to make an active choice," Barnosky said.

"One choice is to acknowledge these issues and potential consequences and try to guide the future (in a way we want to). The other choice is just to throw up our hands and say, 'Let's just go on as usual and see what happens.' My guess is, if we take that latter choice, yes, humanity is going to survive, but we are going to see some effects that will seriously degrade the quality of life for our children and grandchildren."

*The work was supported by UC Berkeley's Office of the Vice Chancellor for Research.*

*Anthony D. Barnosky, Elizabeth A. Hadly, Jordi Bascompte, Eric L. Berlow, James H. Brown, Mikael Fortelius, Wayne M. Getz, John Harte, Alan Hastings, Pablo A. Marquet, Neo D. Martinez, Arne Mooers, Peter Roopnarine, Geerat Vermeij, John W. Williams, Rosemary Gillespie, Justin Kitzes, Charles Marshall, Nicholas Matzke, David P. Mindell, Eloy Revilla, Adam B. Smith. Approaching a state shift in Earth's biosphere. Nature, 2012; 486 (7401): 52 DOI: 10.1038/nature11018*

<http://www.sciencedaily.com/releases/2012/06/120606132302.htm>

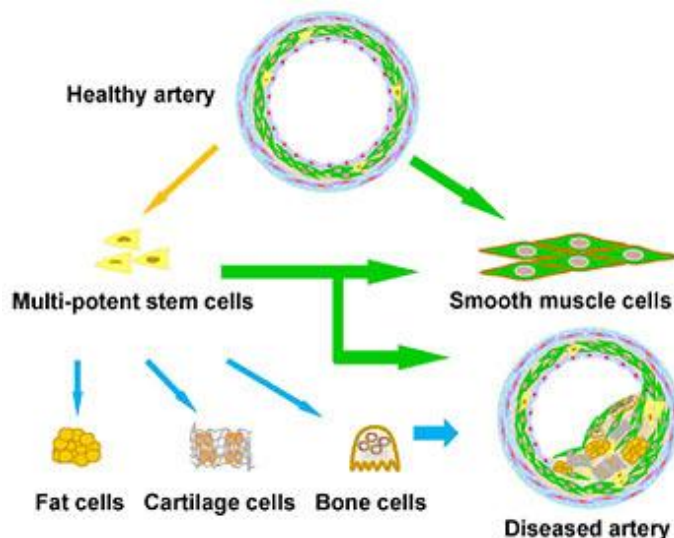
### **The Real Culprit Behind Hardened Arteries? Stem Cells, Says Landmark Study *One of the top suspects behind killer vascular diseases is the victim of mistaken identity, according to researchers from the University of California, Berkeley, who used genetic tracing to help hunt down the real culprit.***

ScienceDaily - The guilty party is not the smooth muscle cells within blood vessel walls, which for decades was thought to combine with cholesterol and fat that can clog arteries. Blocked vessels can eventually lead to heart attacks and strokes, which account for one in three deaths in the United States.

Instead, a previously unknown type of stem cell - a multipotent vascular stem cell - is to blame, and it should now be the focus in the search for new treatments, the scientists report in a new study appearing June 6 in the journal Nature Communications.

"For the first time, we are showing evidence that vascular diseases are actually a kind of stem cell disease," said principal investigator Song Li, professor of bioengineering and a researcher at the Berkeley Stem Cell Center. "This work should revolutionize therapies for vascular diseases because we now know that stem cells rather than smooth muscle cells are the correct therapeutic target." The finding that a stem cell population contributes to artery-hardening diseases, such as atherosclerosis, provides a promising new direction for future research, the study authors said.

"This is groundbreaking and provocative work, as it challenges existing dogma," said Dr. Deepak Srivastava, who directs cardiovascular and stem cell research at the Gladstone Institutes in San Francisco, and who provided some of the mouse vascular tissues used by the researchers. "Targeting the vascular stem cells rather than the existing smooth muscle in the vessel wall might be much more effective in treating vascular disease."



***Within the walls of blood vessels are smooth muscle cells and newly discovered vascular stem cells. The stem cells are multipotent and are not only able to differentiate into smooth muscle cells, but also into fat, cartilage and bone cells.***

***UC Berkeley researchers provide evidence that the stem cells are contributing to clogged and hardened arteries.***  
(Credit: Song Li illustration)

It is generally accepted that the buildup of artery-blocking plaque stems from the body's immune response to vessel damage caused by low-density lipoproteins, the bad cholesterol many people try to eliminate from their diets. Such damage attracts legions of white blood cells and can spur the formation of fibrous scar tissue that accumulates within the vessel, narrowing the blood flow.

The scar tissue, known as neointima, has certain characteristics of smooth muscle, the dominant type of tissue in the blood vessel wall. Because mature smooth muscle cells no longer multiply and grow, it was theorized that in the course of the inflammatory response, they revert, or de-differentiate, into an earlier state where they can proliferate and form matrices that contribute to plaque buildup. However, no experiments published have directly demonstrated this de-differentiation process, so Li and his research team remained skeptical. They turned to transgenic mice with a gene that caused their mature smooth muscle cells to glow green under a microscope.

In analyzing the cells from cross sections of the blood vessels, they found that more than 90 percent of the cells in the blood vessels were mature smooth muscle cells. They then isolated and cultured the cells taken from the middle layer of the mouse blood vessels.

After one month of cell expansion, the researchers saw a threefold increase in the size of the cell nucleus and the spreading area, along with an increase in stress fibers. Notably, none of the new, proliferating cells glowed green, which meant that their lineage could not be traced back to the mature smooth muscle cells originally isolated from the blood vessels.

"Not only was there a lack of green markers in the cell cultures, but we noticed that another type of cell isolated from the blood vessels exhibited progenitor traits for different types of tissue, not just smooth muscle cells," said Zhenyu Tang, co-lead author of the study and a Ph.D. student in the UC Berkeley-UCSF Graduate Program in Bioengineering.

The other co-lead author of the study, Aijun Wang, was a post-doctoral researcher in Li's lab.

"The different phenotypes gave us the clue that stem cells were involved," said Wang, who is now an assistant professor and the co-director of the Surgical Bioengineering Laboratory at the UC Davis Medical Center. "We did further tests and detected proteins and transcriptional factors that are only found in stem cells. No one knew that these cells existed in the blood vessel walls because no one looked for them before."

Further experiments determined that the newly discovered vascular stem cells were multipotent, or capable of differentiating into various specialized cell types, including smooth muscle, nerve, cartilage, bone and fat cells. This would explain why previous studies misidentified the cells involved in vessel clogs as de-differentiated smooth muscle cells after vascular injury. "In the later stages of vascular disease, the soft vessels become hardened and more brittle," said Li. "Previously, there was controversy about how soft tissue would become hard. The ability of stem cells to form bone or cartilage could explain this calcification of the blood vessels."

Other tests in the study showed that the multipotent stem cells were dormant under normal physiological conditions. When the blood vessel walls were damaged, the stem cells rather than the mature smooth muscle cells became activated and started to multiply. The researchers analyzed human carotid arteries to confirm that the same type of multipotent vascular stem cells are found in human blood vessels.

"If your target is wrong, then your treatment can't be very effective," said Dr. Shu Chien, director of the Institute of Engineering in Medicine at UC San Diego, and Li's former adviser. "These new findings give us the right target and should speed up the discovery of novel treatments for vascular diseases."

Grants from the National Institutes of Health and the California Institute for Regenerative Medicine helped support this research.

Zhenyu Tang, Aijun Wang, Falei Yuan, Zhiqiang Yan, Bo Liu, Julia S. Chu, Jill A. Helms, Song Li. *Differentiation of multipotent vascular stem cells contributes to vascular diseases. Nature Communications, 2012; 3: 875 DOI: 10.1038/ncomms1867*

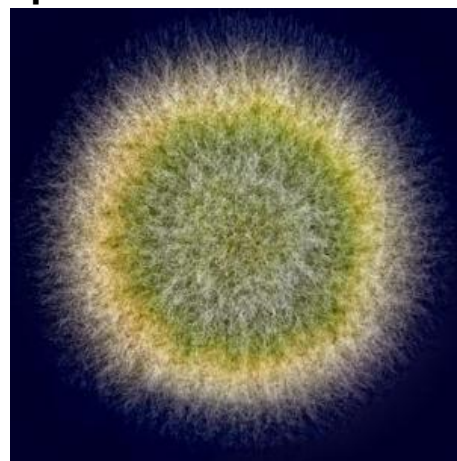
<http://www.sciencedaily.com/releases/2012/06/120606142701.htm>

## Role of Fungus in Digestive Disorders Explored

***Cedars-Sinai researchers say their examination of the fungi in the intestines suggests an important link between these microbes and inflammatory diseases such as ulcerative colitis.***

ScienceDaily - In the new study, published in the June 8 issue of *Science*, researchers at Cedars-Sinai's Inflammatory Bowel and Immunobiology Research Institute identified and characterized the large community of fungi inhabiting the large intestine in a model of the disease.

The digestive tract is home to a large number of micro-organisms. In fact, with an estimated 100 trillion bacteria residing in the gut, microbes outnumber human cells in the body. Some are necessary to aid in digesting food, producing necessary vitamins and suppressing the growth of harmful microbes. Others are harmful to the body, contributing to illnesses such as Crohn's disease, ulcerative colitis and obesity.



***Cedars-Sinai researchers say their examination of the fungi in the intestines suggests an important link between these microbes and inflammatory diseases such as ulcerative colitis.*** (Credit: © Nataliya Hora / Fotolia)

Modern DNA-sequencing technology has revolutionized the study of these microbes in the last decade, allowing the role of bacteria in disease to be understood more clearly, as is shown in the Cedars-Science research published in *Science*.

"It's long been recognized that fungi must also exist in the gut, but we're among the first to investigate what types, how many, and whether they're important in disease," said David Underhill, PhD, associate professor and director of the Graduate Program in Biomedical Science and Translational Medicine, who led the study. "We were truly stunned to see just how common fungi are, identifying more than 100 different types" and seeing linkages to digestive disorders.

An estimated 1.4 million Americans have Inflammatory Bowel Disease, or IBD, a chronic digestive disorder, and about 30,000 new cases are diagnosed annually. Ulcerative colitis, one of the most common types of IBD, causes inflammation and ulcers in the top layers of the lining of the large intestine. Common symptoms include abdominal pain, diarrhea, bleeding, fatigue, weight loss and loss of appetite. Ulcerative colitis patients can be at increased risk of developing colorectal cancer.

"This study takes us an important step closer to understanding how fungi contribute to disease, as well as significantly expanding our understanding of what types of fungi are living in our bodies," said Iliyan Iliev, PhD, a Cedars-Sinai research scientist and lead author on the study.

To determine fungi contribute to inflammatory disease, the study homed in on a protein called Dectin-1, produced by white blood cells and used by the immune system to detect and kill fungi. In an animal model of the disease, researchers found that the protein is important in protecting against inflammation caused by indigenous fungi. The finding has significant implications for human disease, as scientists at the Cedars-Sinai Medical Genetics Institute found a variant of the gene for Dectin-1 that is strongly associated with severe forms of ulcerative colitis.

Iliyan D. Iliev, Vincent A. Funari, Kent D. Taylor, Quoclinh Nguyen, Christopher N. Reyes, Samuel P. Strom, Jordan Brown, Courtney A. Becker, Phillip R. Fleshner, Marla Dubinsky, Jerome I. Rotter, Hanlin L. Wang, Dermot P. B. McGovern, Gordon D. Brown, and David M. Underhill. *Interactions Between Commensal Fungi and the C-Type Lectin Receptor Dectin-1 Influence Colitis. Science, 6 June 2012 DOI: 10.1126/science.1221789*

**Replacing fatty acids may fight MS**  
***Patients lack key lipids that fend off inflammation and nerve damage***  
**By Nathan Seppa**

By delving into the components of protective nerve coatings that get damaged in multiple sclerosis, scientists have identified a handful of lipid molecules that appear to be attacked by an immune system run amok. Bolstering the supply of these lipids might help preserve these nerve coatings and, in the process, knock back the inflammation that contributes to their destruction, researchers report in the June 6 Science Translational Medicine.

In MS patients, rogue antibodies assault myelin, the fatty sheath that insulates nerves and facilitates signaling. Inflammation exacerbates the attack on myelin and the cells that make it. But other details of MS, including the roles of myelin lipids, have been less clearly understood.

“I think this is a very good study,” says Francisco Quintana, an immunologist at Harvard Medical School. “Overall, there are not many papers on lipids in MS. Technically, they are challenging and require a lot of expertise.”

To explore the role of lipids, the researchers studied spinal fluid from people with MS, healthy people and patients with other neurological disorders. Tests on the fluid showed that antibodies targeted four lipids more often in MS patients than in the other groups. Examination of autopsied brains from MS patients and people without MS revealed that, in the MS patients, these four lipids were depleted at the sites where the nerve coatings were damaged.

A nerve needs an intact myelin sheath to conduct signals. “It short-circuits if they are not there,” says study coauthor Lawrence Steinman, a neurologist at Stanford University. This nerve damage causes loss of muscle control and other symptoms characteristic of MS.

Steinman and his colleagues conducted tests in mice with a condition similar to MS and found that injections of the lipids over several weeks could limit severity of the disease and even reverse some symptoms in the animals. The four lipids — abbreviated as PGPC, azPC, azPC ester and POPS — share a similar phosphate group, to which the rogue antibodies bind.

Other tests in mice showed that side chains of fatty acids, attached to the lipids like fingers on a glove, “keep the myelin-making cells alive and reduce the inflammatory response,” Steinman says. “It turns out that the side chains are imbued with protective properties.” They repel inflammation and even kill the T cells that trigger it, the researchers found.

It could be that people with MS, who lack adequate supplies of these lipids and their protective fatty acids, fail to keep up with the destruction caused by antibodies and inflammation. But that dismal numbers game might present an opening for future research, Steinman says. Just as the mice benefited from receiving extra lipids, human patients might, too. And some tests now show that mice can take the lipids orally and still improve, he adds.

Quintana says that further animal studies will be needed to clarify the full effects of giving lipids to fight MS. “But it could potentially lead to some kind of therapy.”

Joan Goverman, an immunologist at the University of Washington in Seattle, says the researchers deserve credit for their approach. “Looking at humans and then going back and incorporating that in animal models is a powerful way to understand the disease.”

<http://bit.ly/MUYGS>

**Antidepressants in water trigger autism genes in fish**  
***Low levels of antidepressants and other psychoactive drugs in water supplies can trigger the expression of genes associated with autism – in fish at least.***

**Updated 16:31 07 June 2012 by Sara Reardon**

The use of antidepressants has increased dramatically over the past 25 years, says Michael Thomas of Idaho State University in Pocatello. Around 80 per cent of each drug passes straight through the human body without being broken down, and so they are present in waste water. In most communities, water purification systems cannot filter out these pharmaceuticals. “They just fly right through,” says Thomas, which means they ultimately find their way into the water supply.

The concentration of these drugs in drinking water is very low – at most, they are present at levels several orders of magnitude lower than the prescription doses. But since the drugs are specifically designed to act on the nervous system, Thomas hypothesised that even a small dose could affect a developing fetus.

Thomas's group created a cocktail of the anti-epileptic drug carbamazepine and two selective serotonin uptake inhibitor (SSRI) antidepressants, fluoxetine and venlafaxine, at this low concentration. They exposed fathead minnows (*Pimephales promelas*) to the drugs for 18 days, then analysed the genes that were being expressed in the fishes' brains.

Although the researchers had expected the drugs might activate genes involved in all kinds of neurological disorders, only 324 genes associated with autism in humans appeared to be significantly altered. Most of these genes are involved in early brain development and wiring.

The finding fits with previous research which had found that pregnant women who take SSRIs are slightly more likely to have autistic children. (Archives of General Psychiatry, DOI: 10.1001/archgenpsychiatry.2011.73).

To test whether these changes actually altered the fish's behaviour, the researchers did an experiment in which they startled the fish. Fish exposed to the drugs tended to panic and behave differently from a control group of fish.

Thomas emphasises that the research is very preliminary – there's no need for pregnant women to worry about their drinking water yet, he says. The researchers next plan to study whether the drugs have a similar effect in mammals. They are testing this by lacing the drinking water of pregnant mice with the low-concentration cocktail. They are also studying water supplies in areas around the country where there are particularly high concentrations of drugs to determine whether the fish – and people – in these areas have autism-like gene expression patterns. *Journal reference: PLoS One, DOI: 10.1371/journal.pone.0032917*

*This article was first posted under a different headline. It has been changed to emphasise that the finding concern fish, not humans. In addition, the description of the concentrations of the drugs in the third paragraph has been edited.*

[http://www.eurekalert.org/pub\\_releases/2012-06/sfts-tto060112.php](http://www.eurekalert.org/pub_releases/2012-06/sfts-tto060112.php)

### **3 types of fetal cells can migrate into maternal organs during pregnancy** ***Some mothers literally carry pieces of their children in their bodies***

A pregnant woman's blood stream contains not only her own cells, but a small number of her child's, as well, and some of them remain in her internal organs long after the baby is born. Understanding the origin and identity of these cells is vital to understanding their potential effects on a mother's long-term health. For example, fetal cells have been found at tumor sites in mothers, but it is unknown whether the cells are helping to destroy the tumor or to speed its growth.

Three types of fetal cells have now been identified in the lungs of late-term pregnant mice by a team led by Dr. Diana Bianchi of Tufts Medical Center. The research, published 6 June 2012 in *Biology of Reproduction's* Papers-in-Press, used publicly available databases to extract important genetic information from as few as 80 fetal cells. A combination of two different analytical techniques to characterize the rare fetal cells revealed a mixed population of trophoblasts (placental cells that provide nutrients to the fetus), mesenchymal stem cells (cells that later develop into fat, cartilage, or bone cells), and immune system cells.

Researchers suspect that fetal cells in a mother's blood stream help her immune system tolerate and not attack the fetus. The detection of trophoblasts and immune cells in the maternal lung should aid future studies on this subject, as well as research into pregnancy-related complications like preeclampsia. The presence of fetal mesenchymal stem cells corresponds with previous studies that reported fetal and placental cells differentiating to repair injured maternal organs in both mice and humans.

Using this team's techniques of gene expression analysis, researchers should now be better able to identify the types of cells present in maternal organs and in doing so determine their potential short- and long-term effects on a mother's internal systems.

*Pritchard S, Wick HC, Slonim DK, Johnson KL, Bianchi DW. Comprehensive analysis of genes expressed by rare microchimeric fetal cells in maternal lung. Biol Reprod 2012; (in press). Published online ahead of print 6 June 2012; DOI 10.1095/biolreprod.112.101147.*

[http://www.eurekalert.org/pub\\_releases/2012-06/luhs-wbf060512.php](http://www.eurekalert.org/pub_releases/2012-06/luhs-wbf060512.php)

### **Why belly fat isn't all bad**

#### ***Fatty membrane helps regulate immune system***

MAYWOOD, Ill. -- A fatty membrane in the belly called the omentum has until recently been considered somewhat like the appendix -- it didn't seem to serve much purpose. But Loyola University Chicago Stritch School of Medicine researchers have found that the omentum appears to play an important role in regulating the immune system. The finding could lead to new drugs for organ transplant patients and patients with auto-immune diseases such as lupus and Crohn's disease. "We now have evidence that the omentum is not just fat sitting in the belly," said Makio Iwashima, PhD, corresponding author of a study published in the June 6 issue of *PLoS ONE*. Iwashima is an associate professor in the Department of Microbiology and Immunology. Here is



a link to the article: <http://dx.plos.org/10.1371/journal.pone.0038368>. The omentum is a membrane that lines the abdominal cavity and covers most abdominal organs. It is a repository for fat tissue.

A research team headed by Iwashima and Robert Love, MD, a world renowned lung transplant surgeon, examined the effect that mouse omentum cells had on T lymphocyte cells from a mouse. T cells are the immune system's first line of defense against infection. They identify, attack and destroy bacteria, viruses and other infectious agents.

Normally, T cells multiply in response to an infectious agent, such as an antibody. But when researchers put omentum cells in with activated T cells that had been exposed to antibodies, the T cells did not multiply as they normally would, but instead died. The omentum cells had this effect only on T cells that had been activated. Omentum cells did not have any effect on inactive T cells.

It appears that omentum cells secrete a substance that tamps down the immune system. This discovery could lead to new drugs that would suppress the immune system with fewer side effects than those caused by immune-suppressing drugs now in use. Such drugs could be used, for example, to suppress the immune system in a patient who has received a lung transplant.

In addition to modulating the immune system, the omentum also appears to play a critical role in regenerating damaged tissues, Iwashima said. The omentum contains mesenchymal stem cells that migrate to the site of an injury and help regenerate tissue. Mesenchymal stem cells are cells that have the ability to develop into various types of specialized cells.

In this study, researchers showed that, in tissue-culture flasks, omentum cells can differentiate into lung-type cells as well as bone cells. Iwashima believes the omentum may be the organ specified for tissue healing and regeneration.

*The study was supported by the National Institutes of Health and Van Kampen Cardiovascular Research Fund.*

*Other co-authors, all at Loyola, are Shivane Shah (first author), Erin Lowery, Rudolf K. Braun, Alicia Martin, Nick Huang, Melissa Medina, Perinann Sethupathi, Yoichi Seki, Mariko Takami, Kathryn Byrne and Christopher Wigfield.*

[http://www.eurekalert.org/pub\\_releases/2012-06/uop-pac060712.php](http://www.eurekalert.org/pub_releases/2012-06/uop-pac060712.php)

## **Penn and Cornell researchers spearhead the development of new guidelines for veterinary CPR**

***While more than 20 percent of human patients who suffer cardiac arrests in the hospital survive to go home to their families, the equivalent figure for dogs and cats is less than 6 percent***

PHILADELPHIA - For nearly 50 years, the American Heart Association, with the help of researchers and physicians from across the nation, has developed and disseminated guidelines on how best to perform cardiopulmonary resuscitation on patients experiencing cardiac arrest. But no such evidence-based guidelines existed in the veterinary world. Perhaps as a result, while more than 20 percent of human patients who suffer cardiac arrests in the hospital survive to go home to their families, the equivalent figure for dogs and cats is less than 6 percent.

Now the Reassessment Campaign on Veterinary Resuscitation, or RECOVER, a collaborative effort of the American College of Veterinary Emergency and Critical Care and the Veterinary Emergency and Critical Care Society, has arrived at the first evidence-based recommendations to resuscitate dogs and cats in cardiac arrest. The RECOVER initiative was spearheaded by Manuel Boller, a senior research investigator in the University of Pennsylvania School of Veterinary Medicine and the Center for Resuscitation Science of Penn's Perelman School of Medicine, and Daniel J. Fletcher, an assistant professor in veterinary emergency and critical care at Cornell University's College of Veterinary Medicine. RECOVER aims to standardize treatment of cardiac arrest in pets, ultimately leading to improved outcomes.

In a special issue of the Journal of Veterinary Emergency and Critical Care published today, a series of articles outlines the new guidelines as well as the method by which they were identified. The articles also include algorithms and drug-dose charts for practitioners to follow.

The need for pet-CPR guidelines became obvious when Boller and colleagues surveyed veterinarians on how they treated dogs and cats in cardiac arrest. The results, compiled from more than 600 practitioners, showed a large amount of variation. "What we found was that there was really no consensus on how to do that best," Boller said. "There may have been a cohort, for example, that recommended 60-80 compressions per minute and another that thought 120-150 compressions per minute was the right thing."

Boller and Fletcher recruited more than 100 board-certified veterinary specialists from around the world who systematically reviewed more than 1,000 scientific papers related to CPR. Weighting the studies by their rigor and relevance to dogs and cats, the committee ended up with 101 specific clinical guidelines. Each has a rating based on the strength of the evidence backing it.

Among the recommended practices:

***Perform 100-120 chest compressions per minute of one-third to one-half of the chest width, with the animal lying on its side.***

***Ventilate intubated dogs and cats at a rate of 10 breaths per minute, or at a compression to ventilation ratio of 30 to 2 for mouth-to-snout ventilation.***

***Perform CPR in 2-minute cycles, switching the "compressor" each cycle.***

***Administer vasopressors every 3 minutes during CPR.***

Other guidelines pertain to how clinicians should be trained, how to perform CPR on dogs of different breeds and sizes, what drugs to give when and what follow-up care to provide.

"We identified two overarching goals for our research: first to devise clinical guidelines establishing how to best treat cardiopulmonary arrest in dogs and cats, and second to identify important knowledge gaps in veterinary CPR that need to be filled in order to improve the quality of recommendations, and thus the quality of patient care in the future," said Fletcher. "With this knowledge we can construct and implement educational initiatives that are evidence-based."

The RECOVER guidelines represent a unique partnership between veterinary experts and physician-scientists who study and treat cardiac arrest in humans. The initiative exemplifies an effort to provide the same evidence-based care for family pets that physicians employ to save human victims of cardiac arrest, which remains one of the nation's leading killers.

"When you look at guidelines for human CPR, they have been heavily informed by research done with animals, which forms the fundamental concepts to build clinical trials on," said Boller, who works closely with leaders of Penn Medicine's Center for Resuscitation Science to develop new techniques for cardiac arrest treatment. "Now, what we're doing is turning things around by using the clinical research that was conducted in humans to inform how we should do CPR to help our animals. It's really getting something back from this process of helping humans."

By identifying the gaps in knowledge of how to best perform CPR, Boller said, RECOVER should inspire new research. "Ultimately I hope RECOVER will lead to novel interventions and really move the field forward," he said.

Using the new guidelines, the RECOVER team is developing an Internet-based training curriculum to certify clinicians in veterinary CPR. This certification is being peer-reviewed by the American College of Veterinary Emergency and Critical Care, much as the training materials for human CPR are accredited by the American Heart Association. The guidelines will be updated regularly, with the next RECOVER planned for 2017.

[http://www.eurekalert.org/pub\\_releases/2012-06/elar-twa\\_1053112.php](http://www.eurekalert.org/pub_releases/2012-06/elar-twa_1053112.php)

## **Treatment with anti-TNFs can increase the risk of shingles by up to 75 percent**

### ***Results of a systematic review urge prophylactic treatment for those at risk***

Berlin, Germany - Patients with inflammatory rheumatic diseases (IRD) treated with anti-tumour necrosis factor medications (anti-TNFs) have a 75% greater risk of developing herpes zoster, or shingles, than patients treated with traditional disease modifying anti-rheumatic drugs (DMARDs), according to a meta-analysis presented today at EULAR 2012, the Annual Congress of the European League Against Rheumatism.

"Anti-TNFs, such as infliximab, adalimumab and etanercept have become the treatment of choice for patients with inflammatory rheumatic diseases who are uncontrolled on traditional DMARDs, but it is known that a side effect of these drugs is an increased risk of bacterial infections," said Ms. Helene Che, from Lapeyronie Hospital, France and lead author of the study. "This systematic review and meta-analysis demonstrates that careful monitoring of patients treated with anti-TNFs is required for early signs and symptoms of herpes zoster and raises the issue as to when vaccination against the virus should occur."

The study authors conducted a literature search in Medline, Embase, the Cochrane library and abstracts from ACR and EULAR congresses from 2006 to 2010. From the 657 articles, 134 congress abstracts, and 11 national registries included in the literature search, 22 articles and 28 abstracts met eligibility criteria and were included in the study. The meta-analysis included a total follow up of 124,966 patient years (PY) (74,198 PY in the biologics group and 50,768 PY in the DMARD group) across five registries.

Studies were included in the meta-analysis if they reported the respective incidences of herpes infection in anti-TNF and conventional DMARD treated patients. Incidence of severe herpetic infections (multidermatomal lesions, requiring hospitalisation or intravenous treatment) were excluded and reported when available.

Herpes zoster, also known as shingles, is a painful, blistering skin rash due to the varicella-zoster virus, the same virus that causes chickenpox. People are more likely to develop it if they are older than 60, had chickenpox before the age of one and have a compromised immune system due to medications or disease.

Symptoms include one-sided pain, tingling or burning followed by a rash of small blisters, which eventually break, ulcer and dry up. Other symptoms may include fever, chills, abdominal pain, swollen glands, difficulty moving muscles in the face, and drooping eyelids. Shingles is usually treated with antiviral medications to reduce pain and complications and corticosteroids to reduce swelling. Pain from shingles can last for months or years, even though the infection normally lasts only two to three weeks. The virus can also cause temporary or permanent paralysis. \*Abstract Number: THU0368 \*Netdoctor - Shingles (Herpes zoster).

<http://www.netdoctor.co.uk/diseases/facts/herpeszoster.htm> 2011.

[http://www.eurekalert.org/pub\\_releases/2012-06/ki-avt060712.php](http://www.eurekalert.org/pub_releases/2012-06/ki-avt060712.php)

### **Alzheimer's vaccine trial a success**

#### ***A study led by Karolinska Institutet in Sweden reports for the first time the positive effects of an active vaccine against Alzheimer's disease.***

The new vaccine, CAD106, can prove a breakthrough in the search for a cure for this seriously debilitating dementia disease. The study is published in the distinguished scientific journal *Lancet Neurology*.

Alzheimer's disease is a complex neurological dementia disease that is the cause of much human suffering and a great cost to society. According to the World Health Organisation, dementia is the fastest growing global health epidemic of our age. The prevailing hypothesis about its cause involves APP (amyloid precursor protein), a protein that resides in the outer membrane of nerve cells and that, instead of being broken down, form a harmful substance called beta-amyloid, which accumulates as plaques and kills brain cells.

There is currently no cure for Alzheimer's disease, and the medicines in use can only mitigate the symptoms. In the hunt for a cure, scientists are following several avenues of attack, of which vaccination is currently the most popular. The first human vaccination study, which was done almost a decade ago, revealed too many adverse reactions and was discontinued. The vaccine used in that study activated certain white blood cells (T cells), which started to attack the body's own brain tissue.

The new treatment, which is presented in *Lancet Neurology*, involves active immunisation, using a type of vaccine designed to trigger the body's immune defence against beta-amyloid. In this second clinical trial on humans, the vaccine was modified to affect only the harmful beta-amyloid. The researchers found that 80 per cent of the patients involved in the trials developed their own protective antibodies against beta-amyloid without suffering any side-effects over the three years of the study. The researchers believe that this suggests that the CAD106 vaccine is a tolerable treatment for patients with mild to moderate Alzheimer's. Larger trials must now be conducted to confirm the CAD106 vaccine's efficacy.

*The study was carried out by Professor Bengt Winblad at Karolinska Institutet's Alzheimer's Disease Research Centre in Huddinge and leading neurologists in the Swedish Brain Power network: consultant Niels Andreasen from Karolinska University Hospital, Huddinge; Professor Lennart Minthon from the MAS University Hospital, Malmö; and Professor Kaj Blennow from the Sahlgrenska Academy, Gothenburg. The study was financed by Swiss pharmaceutical company Novartis. Publication: "Safety, tolerability, and antibody response of active A $\beta$ immunotherapy with CAD106 in patients with Alzheimer's disease: randomised, double-blind, placebo-controlled, first-in-human study", Bengt Winblad, Niels Andreasen, Lennart Minthon, Annette Floesser, Georges Imbert, Thomas Dumortier, R Paul Maguire, Kaj Blennow, Joens Lundmark, Matthias Staufenbiel, Jean-Marc Orgogozo & Ana Graf, *Lancet Neurology*, online first 6 June 2012, doi:10.1016/S1474-4422(12)70140-0.*

[http://www.eurekalert.org/pub\\_releases/2012-06/hcfo-hdd060712.php](http://www.eurekalert.org/pub_releases/2012-06/hcfo-hdd060712.php)

### **How does dolomite form?**

#### ***Scientists in Kiel show the influence of marine bacteria on mineral formation***

Not only in the Dolomites, but throughout the world dolomite is quite common. More than 90 percent of dolomite is made up of the mineral dolomite. It was first described scientifically in the 18th century. But who would have thought that the formation of this mineral is still not fully understood, although geologists are aware of large deposits of directly formed (primary) dolomite from the past 600 million years. The process of recent primary dolomite formation is restricted to extreme ecosystems such as bacterial mats in highly saline lakes and lagoons. "As these systems are very limited in space, there is an explanation gap for geologists for the widespread presence of fossil dolomite," explains Dr. Stefan Krause, Geomicrobiologist at GEOMAR | Helmholtz Centre for Ocean Research Kiel.

A team of biologists and geochemists, who are conducting research together in the Cluster of Excellence "Future Ocean", in collaboration with colleagues at the ETH Zurich and the Centro de Madrid Astrobiología, have now brought a little light into the darkness of this scientific riddle. Their findings are published in the advance online issue of the international journal "Geology".

In simple laboratory experiments with globally distributed marine bacteria which use sulphur compounds instead of oxygen for energy production (sulfaterespiration), the scientists were able to demonstrate the

formation of primary dolomite crystals under conditions that prevail today in marine sediments. "The dolomite precipitates exclusively within a mucus matrix, secreted by the bacteria to form biofilms," says Stefan Krause, for whom this study is an important part of his PhD thesis. "Different chemical conditions prevail within the biofilm compared to in the surrounding water. In particular, the alteration of the magnesium to calcium ratio plays an important role. These changes allow for the formation of dolomite crystals. "

The study has provided further insight. "We were able to show that the ratio of different isotopes of calcium between the ambient water, the biofilm and dolomite crystals is different," explains Dr. Volker Liebetrau from GEOMAR. "This ratio is an important tool for us to reconstruct past environmental conditions. The fact that bacteria are involved in this process allows more precise interpretations of climate signals that are stored in rocks. "

Evidence of primary dolomite formation by a process as common as microbial sulphate respiration under conditions that currently prevail in the seabed, provides new insights into the reconstruction of fossil dolomite deposits. But why are large scale deposits from primary dolomite no longer formed at the ocean floor? "Here we are still faced with a puzzle," says Professor Tina Treude, head of the Working Group at GEOMAR. "One possibility is that massive primary dolomite can form particularly during times when large quantities of organic matter in the seabed are degraded by sulfate-respiring bacteria. Such conditions exist when the sea water above the seafloor is free of oxygen. In Earth's history, several such oxygen-free periods have occurred, partly consistent with time periods of intensified dolomite deposition. "

Krause, S., V. Liebetrau, S. Gorb, M. Sánchez-Román, J.A. McKenzie, T. Treude, 2012: *Microbial nucleation of Mg-rich dolomite in exopolymeric substances under anoxic modern seawater salinity: New insight into an old enigma. Geology*, <http://dx.doi.org/10.1130/G32923.1>

<http://phys.org/news/2012-06-people-undocumented-immigrants-crime.html>

### **Why people believe undocumented immigrants cause more crime**

***ASU criminologist Xia Wang examined why people believe undocumented immigrants are responsible for more crime than they commit.***

Phys.org - Xia Wang wanted to find out why so many Americans believe undocumented immigrants commit more crime.

"The weight of evidence suggests that immigration is not related to more crime," said Wang, an assistant professor in the School of Criminology and Criminal Justice at Arizona State University. "But this body of scholarship doesn't seem to affect the public's perception. The public consistently perceives immigrants, especially undocumented immigrants, as criminal."

To better understand why that perception exists, Wang used data from a poll of more than 1,000 people in Arizona, New Mexico, Nevada, and Texas. She applied the minority threat perspective, a theory that seeks to explain why minorities are treated differently by law enforcement. The results were published last month in an article that appeared online in the journal *Criminology*. Wang found the belief that undocumented immigrants cause crime was due in part to the perceived population size of the immigrant community overall.

"If somebody is perceiving undocumented immigrants as a larger proportion in the population, they are going to perceive undocumented immigrants at a higher level of criminal threat," Wang said. "And what's interesting is a lot of people have very distorted and exaggerated views of the population size of undocumented immigrants."

The data show a large proportion of respondents estimated the undocumented population to be more than half of the overall foreign born population, far greater than recognized statistics. In 2011, the Census Bureau's Current Population Survey listed the U.S. immigrant population at 39.6 million, while the Pew Hispanic Center estimated 28%, or 11.2 million, were unauthorized immigrants.

"As for why people have very distorted, exaggerated views, what I found is that individual factors such as your level of education and your victimization experience shape your views," said Wang. "It's a bit surprising to me because I would think that people would form their perceptions of undocumented immigrant population size based on the conditions their neighborhood is in, such as the actual size of the immigrant population."

Wang tested to see if the economic condition, or unemployment rate of respondents' communities played a role in believing undocumented immigrants were more involved in crime. It didn't for the general population, but it did for the native born.

"Those neighborhood conditions don't matter as much," Wang said. "It is largely the individual characteristics that shape people's perceptions of undocumented immigrants population size and perceptions of undocumented immigrants as more criminal."

Wang said that for criminologists her analysis shows the minority threat perspective could be applied to undocumented immigrants.

For members of the public, she hoped it may lead them to ask why undocumented immigrants are perceived as causing more crime. "They actually commit less crime than the native born. But why do we consistently believe they are more criminal?" asked Wang. "We can ask ourselves and be more critical of our views. Are we being reasonable? Are we being rational?"

<http://phys.org/news/2012-06-cyber-experts-intelligent-weapons.html>

### **Cyber experts warn of 'intelligent weapons'**

#### ***Quick advances in cyber war technologies could soon lead to a new generation of so-called "intelligent cyber weapons"***

Quick advances in cyber war technologies could soon lead to a new generation of so-called "intelligent cyber weapons" which top global IT defence experts warn could be virtually unstoppable.

Quick advances in cyber war technologies could soon lead to a new generation of so-called "intelligent cyber weapons" which top global IT defence experts warn could be virtually unstoppable.

"Rapid developments in cyber (technology) might lead to intelligent cyber weapons that are hard to control and it's practically impossible to use formal methods of verifying the safety of intelligent cyber weapons by their users," Enn Tyugu, IT expert at Tallinn's NATO Cyber Defence Centre said at its fourth annual conference Thursday.

He also warned that programmes developed to counter attacks by malwares like Stuxnet can act independently and could possibly themselves spark conflicts. "They are quite autonomous, and can operate independently in an unfriendly environment and might at some point become very difficult to control... that can lead to cyber conflict initiated by these agents themselves," Tyugu said.

"Stuxnet and Flame have shown the side of cyber of which the average user does not think of but which will bring a lot of challenges to all experts who deal with critical infrastructure protection issues - IT experts, lawyers, policy makers," Ilmar Tamm, Head of the NATO Cyber Defence Centre told AFP Thursday.

"The number of cyber conflicts keeps rising and it is important to understand who the actors in these events are, how to classify these events and participants, and how to interpret all that," Tamm said, noting Western leaders have been slow to become aware of even existing cyber threats.

Experts at the conference noted that both China and Russia have significantly upgraded their cyber-defence capabilities in recent years by creating new IT units.

"But the most powerful weapon today in cyber space is still the propaganda, the chance to use the Internet to spread your message," Kenneth Geers, US cyber defence expert told some 400 top IT gurus attending the meeting Thursday.

Keir Giles, head of Oxford University's Conflict Studies Research Centre, noted that some Russian leaders seemed to "sincerely believe that the recent opposition rallies after the presidential elections in Russia were initiated by the US in cyberspace."

<http://www.bbc.co.uk/news/health-18356045>

### **Spine manipulation for neck pain 'inadvisable'**

#### ***A common chiropractic treatment for neck pain, which involves applying thrusts to the neck area of the spine, should be abandoned, say experts.***

Writing in the British Medical Journal, Neil O'Connell and colleagues say that cervical spine manipulation carries a low risk of stroke, resulting from damage to the major neck arteries. They say the technique is "unnecessary and inadvisable".

But other experts believe it is a valuable addition to patient care. Spinal manipulation can be used to treat neck and back pain or other musculoskeletal conditions. It is a technique used by physiotherapists, osteopaths and most commonly by chiropractors.

Cervical spine manipulation focuses on the neck and involves a range of high-speed manual manoeuvres that stretch, mobilise or manipulate the upper spine in order to relieve pain.

#### **'Serious complications'**

Neil O'Connell, from the Centre for Research and Rehabilitation at Brunel University and colleagues argue that cervical spine manipulation "may carry the potential for serious neurovascular complications".

They also say that studies "provide consistent evidence of an association between neurovascular injury and recent exposure to cervical manipulation." Such injuries include tearing the lining of the vertebral artery, which is located in the neck and supplies blood to the brain, and stroke.

O'Connell and colleagues refer to a Cochrane review of randomised trials of neck manipulation or mobilisation which found that as a stand-alone treatment, the technique provides only moderate short-term pain relief. They point to other recent, high-quality trials which suggest that manipulation is no better than other treatments such as physical exercise.

In their view, the risks of using manipulation for neck pain outweigh the benefits. They conclude: "The potential for catastrophic events and the clear absence of unique benefit lead to the inevitable conclusion that manipulation of the cervical spine should be abandoned as part of conservative care for neck pain."

### **Safe treatment**

However, not all experts agree.

Writing in the same edition of the BMJ, Professor David Cassidy, from the University of Toronto, and colleagues argue that cervical spine manipulation should not be abandoned as a treatment for neck pain.

They point to high quality evidence that "clearly suggests that manipulation benefits patients with neck pain" and raises doubt about any direct relation between manipulation and stroke.

But they want to see more research into the pros and cons of this and other techniques with the aim of identifying safe and effective treatments.

The British Chiropractic Association said chiropractors were highly trained in spine care.

"The cherry-picking of poor quality research needlessly raises alarm in patients and does little to help the people suffering from neck pain and headaches to choose the most appropriate treatment," it said.

<http://bit.ly/LgkTgM>

### **Plants may be able to 'hear' others**

#### ***THEY can "smell" chemicals and respond to light, but can plants hear sounds?***

**08 June 2012 by Michael Marshall**

It seems chilli seeds can sense neighbouring plants even if those neighbours are sealed in a box, suggesting plants have a hitherto-unrecognised sense.

Plants are known to have many of the senses we do: they can sense changes in light level, "smell" chemicals in the air and "taste" them in the soil (New Scientist, 26 September 1998, p 24). They even have a sense of touch that detects buffeting from strong winds.

The most controversial claim is that plants can hear, an idea that dates back to the 19th century. Since then a few studies have suggested that plants respond to sound, prompting somewhat spurious suggestions that talking to plants can help them grow.

A team led by Monica Gagliano at the University of Western Australia in Crawley placed the seeds of chilli peppers (*Capsicum annuum*) into eight Petri dishes arranged in a circle around a potted sweet fennel plant (*Foeniculum vulgare*).

Sweet fennel releases chemicals into the air and soil that slow other plants' growth. In some set-ups the fennel was enclosed in a box, blocking its chemicals from reaching the seeds. Other experiments had the box, but no fennel plant inside. In each case, the entire set-up was sealed in a soundproof box to prevent outside signals from interfering.

As expected, chilli seeds exposed to the fennel germinated more slowly than when there was no fennel. The surprise came when the fennel was present but sealed away: those seeds sprouted fastest of all.

Gagliano repeated the experiment with 2400 chilli seeds in 15 boxes and consistently got the same result, suggesting the seeds were responding to a signal of some sort (PLoS One, DOI: 10.1371/journal.pone.0037382). She believes this signal makes the chilli seeds anticipate the arrival of chemicals that slow their growth.

In preparation, they undergo a growth spurt. The box surrounding the fennel would have blocked chemical signals, and Gagliano suggests sound may be involved.

In a separate experiment, chilli seeds growing next to a sealed-off chilli plant also consistently grew differently to seeds growing on their own, suggesting some form of signalling between the two.

Though the research is at an early stage, the results are worth pursuing, says Richard Karban of the University of California-Davis. They do suggest that plants have an as-yet-unidentified means of communication, he says, though it is not clear what that might be.

The key question is whether the boxes around the fennel plants really block all known signals, says Susan Dudley of McMaster University in Hamilton, Ontario, Canada. She concedes that plants make faint noises when water columns in their stems are disrupted, and that hearing functions in much the same way as the sense of touch - which plants have - but wants to see the results replicated before she is convinced that plants can hear. The study, she says, comes as a challenge to botanists to either refute or confirm.

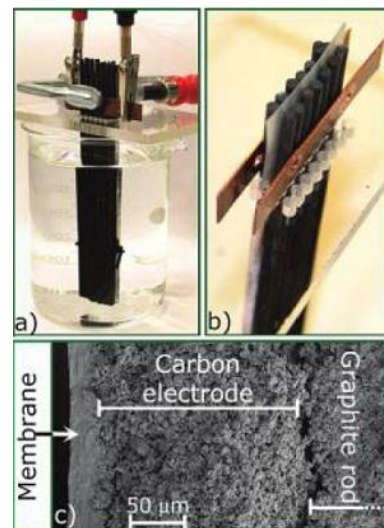
## Wires turn salt water into freshwater

**As a rising global population and increasing standard of living drive demand for freshwater, many researchers are developing new techniques to desalinate salt water.**

Phys.org - Among them is a team of scientists from The Netherlands, who have shown how to transform brackish (moderately salty) water into potable freshwater using just a pair of wires and a small voltage that can be generated by a small solar cell. The simple technique has the potential to be more energy-efficient than other techniques because of the minimal amount of mixing between the treated and untreated water.

The researchers, led by Maarten Biesheuvel from Wageningen University in Wageningen, The Netherlands, and Wetsus, Centre of Excellence for Sustainable Water Technology in Leeuwarden, The Netherlands, have published their study on water desalination with wires in a recent issue of *The Journal of Physical Chemistry Letters*.

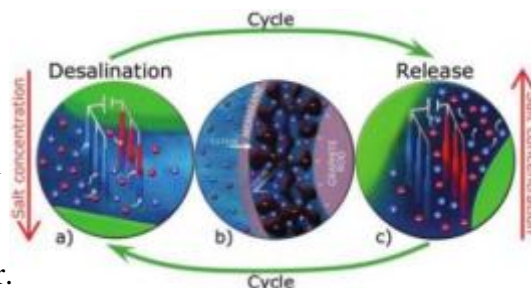
As the researchers explain in their study, there are two main ways to desalinate salt water. One way is to remove pure water molecules from the salt water, as done in distillation and reverse osmosis, particularly for water with a high salt concentration. The opposite approach is to remove the salt ions from the salt water to obtain freshwater, which is done in deionization and desalination techniques using, among other things, batteries and microbial cells.



**(a) Seven pairs of graphite rods/wires are dipped into brackish water. (b) An electrical voltage difference is applied between the anode and cathode wires via copper strips, causing the electrodes to adsorb salt ions. (c) Scanning electron microscopy image of the membrane-electrode assembly.** Image credit: S. Porada, et al. ©2012 American Chemical Society

Here, the scientists used the second approach, in which they removed positively charged sodium ions and negatively charged chlorine ions from brackish water to produce freshwater. To do this, they designed a device consisting of two thin graphite rods or wires, which are inexpensive and highly conductive. Then they coated the outer surface of the wires with a porous carbon electrode layer so that one wire could act as a cathode and one as an anode. The wires were clamped a small distance apart in a plastic holder, with each wire squeezed against a copper strip.

To activate the electrodes, the researchers dipped seven sets of wire pairs into a container of brackish water and ran electrical wires from the copper strips to an external power source. Upon applying a small voltage difference (1-2 volts) between the two graphite wires of each wire pair, one wire became the cathode and adsorbed the positively charged sodium cations, while the other wire became the anode and adsorbed the negatively charged chlorine anions from the salty water.



**(a) Multiple pairs of porous electrode wires adsorb salt ions under an applied voltage. (b) A porous electrode temporarily stores ions as the device is carried to the brine container. (c) After short-circuiting the cells, salt is released in the brine container, and the wires are transferred back to the freshwater container.** Image credit: S. Porada, et al. ©2012 American Chemical Society

The ions are temporarily stored inside the nanopores of the carbon electrode coating until the wire pair is manually lifted from the once-treated solution and dipped into another container of waste water, or brine. Then the researchers removed the voltage, which caused the electrodes to release the stored ions into the waste water, increasing its salinity. By repeating this cycle eight times, the researchers measured that the salt concentration of the original brackish water, 20 mM (millimolars), is reduced to about 7 mM. Potable water is considered to have a salinity of less than roughly 15 mM. As Biesheuvel explained, this improvement could be useful for applications involving the treatment of moderately salty water.

“The new technique is not so suitable for extremely salty waters, as it is based on removing the salt, and making the remaining water less salty,” Biesheuvel told Phys.org, explaining that distillation and reverse osmosis are still superior for desalinating seawater (500 mM salinity and higher). “The new technique is more suitable, for example, for groundwater, or for water for consumer applications that needs to be treated to remove so-called ‘hardness ions’ and make it less saline. These water streams are less saline to start with, say 100 mM or 30 mM. Or this new approach can be of use to treat water in industry to remove ions (salts) that slowly accumulate in

the process. In this way there is no need anymore to take in freshwater and/or to dump used water (at high financial penalty).”

One of the biggest advantages of the technique is that it avoids inadvertently mixing the brine with the water being treated during the process, which limits the efficiency of other deionization techniques. By using a handheld wire-based device and producing freshwater in a continuous stream, the researchers could split the two types of water in separate containers to avoid mixing. Only a minimal amount of brine, about 0.26 mL per electrode, is transferred between containers, which does limit the degree of desalination but to a lesser extent than other techniques. Another advantage of the new technique is that it has the potential to be less expensive than other desalination methods.

“This technique can be made very inexpensive, just carbon rods or wires to conduct the electrons, onto which you can simply ‘paint’ the activated carbon slurry, which becomes the porous carbon electrode,” Biesheuvel said. “Because of its simplicity and low cost, it might out-compete state-of-the-art technologies for certain applications, and may also have advantages over the technology called capacitive deionization (CDI or cap-DI), which is beyond the development stage and commercially available. Also, the voltage required is low, just 1.2 V for instance, and DC, perfectly compatible with solar panels. Thus it can be used at off-grid or remote locations.”

In addition, Biesheuvel explained that the wire pairs can be used repeatedly without degradation, which could give the device a long lifetime.

“In capacitive techniques where the porous carbon electrodes are used to capture ions and release them again (in the so-called ‘electrical double layers,’ or EDLs, formed in the very small pores inside the carbon), it is well-known that the cycle can be used for thousands or tens of thousands of times (until the experimenter gets tired) without any appreciable decay,” he said. “For the wires we only went up to six times repeat and found, as expected, no changes. This is in contrast to battery-style techniques, either for energy storage or desalination, where one would expect to lose performance (like rechargeable batteries, which can only be charged, say, 100 times successfully). That is because in those techniques there is real chemistry going on, phase changes, change of the micromorphology of the anode/cathode materials. Here, in the wire desalination technology, nothing of that kind, the EDL is a purely physical phenomenon where ions are stored close to the charged carbon in the nanopores under the action of the applied voltage, and later released again.”

The researchers also found that the efficiency could be improved by adding a second membrane coating to the electrodes. For instance, a cationic membrane on the cathode wire has a high selectivity toward sodium cations while blocking the desorption of chlorine anions from within the electrode region. As a result, cationic (and, on the anode wire, anionic) membranes could enable the electrodes to adsorb and remove more ions than before. In the future, the researchers plan to perform additional experiments using the cationic and anionic membranes. They predict that these improvements could increase the desalination factor from 3 to 4 after eight cycles, with 80% of the water being recovered (i.e., 20% of the original water becomes brine). The researchers also want to use the technique to treat large volumes of water, which they say could be done by using many wire pairs in parallel to accelerate the desalination process.

“This research continues by scaling up the technology (testing larger arrays of wires), packing them more closely, and trying our hand on automation to have the rods lifted automatically from one water stream into another,” Biesheuvel said. “We also want to test ‘real’ ground/surface waters, not only artificial simple salt mixtures as tested now.”

More information: S. Porada, et al. “Water Desalination with Wires.” *The Journal of Physical Chemistry Letters*. DOI: 10.1021/jz3005514

<http://news.discovery.com/animals/dogs-sadness-120608.html>

### **Dogs Know When You're Sad**

***Our canine friends are more likely to approach a crying person than someone who seems happy.***

**Content provided by Stephanie Pappas, LiveScience**

Plenty of pet owners are comforted by a pair of puppy-dog eyes or a swipe of the tongue when their dog catches them crying. Now, new research suggests that dogs really do respond uniquely to tears. But whether pets have empathy for human pain is less clear.

In a study published online May 30 in the journal *Animal Cognition*, University of London researchers found that dogs were more likely to approach a crying person than someone who was humming or talking, and that they normally responded to weeping with submissive behaviors.

The results are what you might expect if dogs understand our pain, the researchers wrote, but it's not proof that they do.



"The humming was designed to be a relatively novel behavior, which might be likely to pique the dogs' curiosity," study researcher and psychologist Deborah Custance said in a statement. "The fact that the dogs differentiated between crying and humming indicates that their response to crying was not purely driven by curiosity. Rather, the crying carried greater emotional meaning for the dogs and provoked a stronger overall response than either humming or talking."

Humans domesticated dogs at least 15,000 years ago, and many a pet owner has a tale of their canine offering comfort in tough times. Studies have shown that dogs are experts at human communication, but scientists haven't been able to show conclusively that dogs feel empathy or truly understand the pain of others. In one 2006 study, researchers had owners fake heart attacks or pretend to be pinned beneath furniture, and learned that pet dogs failed to go for help (so much for Lassie saving Timmy from the well).

But seeking out assistance is a complex task, and Custance and her colleague Jennifer Mayer wanted to keep it simple. They recruited 18 pet dogs and their owners to test whether dogs would respond to crying with empathetic behaviors. The dogs included a mix of mutts, Labrador retrievers, golden retrievers and a few other common breeds. [What Your Dog's Breed Says About You]

The experiment took place in the owners' living rooms. Mayer would arrive and ignore the dog so that it would have little interest in her. Then she and the owner would take turns talking, fake-crying and humming. Of the 18 dogs in the study, 15 approached their owner or Mayer during crying fits, while only six approached during humming. That suggests that it's emotional content, not curiosity, that brings the dogs running. Likewise, the dogs always approached the crying person, never the quiet person, as one might expect if the dog was seeking (rather than trying to provide) comfort.

"The dogs approached whoever was crying regardless of their identity. Thus they were responding to the person's emotion, not their own needs, which is suggestive of empathic-like comfort-offering behavior," Mayer said in a statement.

Of the 15 dogs that approached a crying owner or stranger, 13 did so with submissive body language, such as tucked tails and bowed heads, another behavior consistent with empathy (the other two were alert or playful). Still, the researchers aren't dog whisperers, and they can't prove conclusively what the dogs were thinking. It's possible that dogs learn to approach crying people because their owners give them affection when they do, the researchers wrote.

"We in no way claim that the present study provides definitive answers to the question of empathy in dogs," Mayer and Custance wrote. Nevertheless, they said, their experiment opens the door for more study of dogs' emotional lives, from whether different breeds respond to emotional owners differently to whether dogs understand the difference between laughter and tears.

<http://www.sciencedaily.com/releases/2012/06/120610054737.htm>

### **Mapping Volcanic Heat On Jupiter's Moon Io**

***A new study finds that the pattern of heat coming from volcanoes on Io's surface disposes of the generally-accepted model of internal heating.***

ScienceDaily - The heat pouring out of Io's hundreds of erupting volcanoes indicates a complex, multi-layer source. These results come from data collected by NASA spacecraft and ground-based telescopes and appear in the June issue of the journal *Icarus*.

A map of hot spots, classified by the amount of heat being emitted, shows the global distribution and wide range of volcanic activity on Io. Most of Io's eruptions dwarf their contemporaries on Earth.

"This is the most comprehensive study of Io's volcanic thermal emission to date," said Glenn Veeder of the Bear Fight Institute, Winthrop, Wash., who led the work of a multi-faceted team that included Ashley Davies, Torrence Johnson and Dennis Matson of NASA's Jet Propulsion Laboratory, Pasadena, Calif., Jani Radebaugh of Brigham Young University, in Provo, Utah, and David Williams of Arizona State University, Tempe, Ariz. The team examined data primarily from the NASA's Voyager and Galileo missions, but also incorporated infrared data obtained from telescopes on Earth.

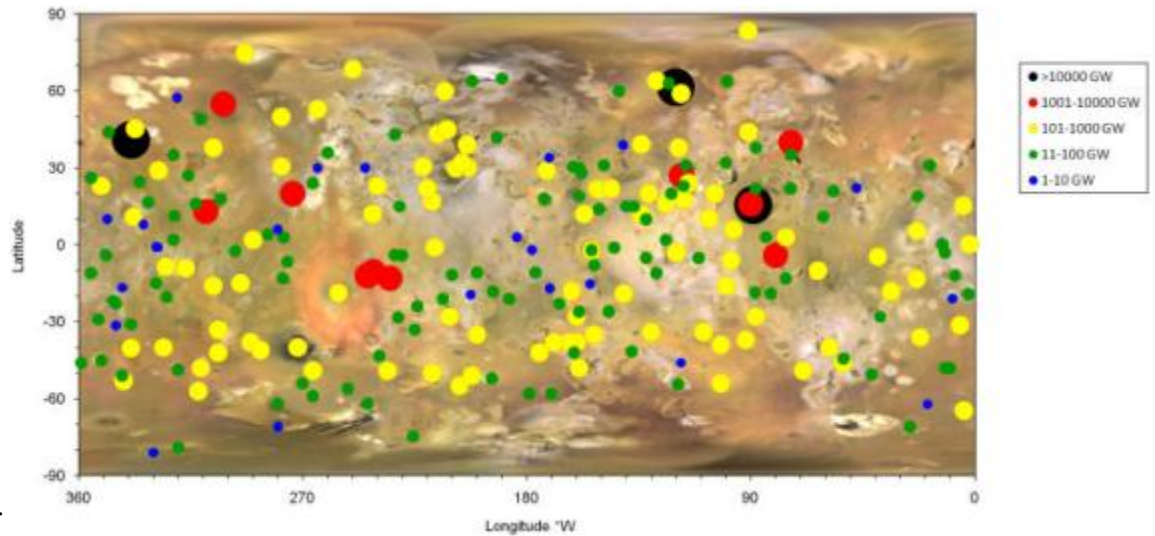
"The fascinating thing about the distribution of the heat flow is that it is not in keeping with the current preferred model of tidal heating of Io at relatively shallow depths," said Davies. "Instead, the main thermal emission occurs about 40 degrees eastward of its expected positions."

"The pattern that emerges points to a complex heating process within Io," said Matson. "What we see indicates a mixture of both deep and shallow heating."

A mystery has also emerged. The team found that active volcanoes accounted for only about 60 percent of Io's heat. This component mostly emanates from flat-floored volcanic craters called paterae, a common feature on Io. But where is the "missing" 40 percent? "We are investigating the possibility that there are many smaller volcanoes that are

hard, but not impossible, to detect," said Veeder. "We are now puzzling over the observed pattern of heat flow."

Understanding this will help identify the tidal heating mechanisms not only within Io, but also may apply to neighboring Europa, a high-priority target for NASA in its search for life beyond Earth.



*Thermal emission from erupting volcanoes on the jovian moon, Io. A logarithmic scale is used to classify volcanoes on the basis of thermal emission: the larger the spot, the larger the thermal emission. Credit: NASA/JPL-Caltech/Bear Fight Institute*

The Galileo mission was managed by NASA's Jet Propulsion Laboratory in Pasadena, Calif., for the agency's Science Mission Directorate. The mission was launched by the space shuttle Atlantis in 1989 to Jupiter, produced numerous discoveries and provided scientists decades worth of data to analyze. Galileo was the first spacecraft to directly measure Jupiter's atmosphere with a probe and conduct long-term observations of the Jovian system. NASA extended the mission three times to take advantage of Galileo's unique science capabilities, and the spacecraft was put on a collision course into Jupiter's atmosphere in September 2003 to eliminate any chance of impacting Europa.

JPL is a division of the California Institute of Technology in Pasadena.

For more information about the Galileo mission, visit: <http://solarsystem.nasa.gov/galileo/>.

Glenn J. Veeder, Ashley Gerard Davies, Dennis L. Matson, Torrence V. Johnson, David A. Williams, Jani Radebaugh. *Io: Volcanic thermal sources and global heat flow. Icarus, 2012; 219 (2): 701 DOI: 10.1016/j.icarus.2012.04.004*

[http://www.eurekalert.org/pub\\_releases/2012-06/eso-abh060612.php](http://www.eurekalert.org/pub_releases/2012-06/eso-abh060612.php)

**Aspirin before heart surgery reduces the risk of post-operative acute kidney failure**  
**Aspirin taken for five days before a heart operation can halve the numbers of patients developing post-operative acute kidney failure**

Paris, France: Aspirin taken for five days before a heart operation can halve the numbers of patients developing post-operative acute kidney failure, according to research presented at the European Anaesthesiology Congress in Paris today (Sunday).

Professor Jianzhong Sun (MD, PhD), professor and attending anaesthesiologist at Jefferson Medical College, Thomas Jefferson University (Philadelphia, USA), told the meeting that in a study of 3,219 patients, pre-operative aspirin therapy was associated with a reduction in acute renal failure of about three in every 100 patients undergoing coronary artery bypass graft (CABG), valve surgery or both.

The patients were divided into two groups: those taking aspirin within five days before their operation (2,247 patients) and those not taking it (972 patients) [1]. Although the researchers had no record of the precise dose taken, doses of between 80-325mg per day is the normal dose for aspirin that is taken over a period of time.

After adjusting their results for various differing characteristics such as age, disease, and other medications, the researchers found that pre-operative aspirin was associated with a significant decrease in the incidence of post-operative kidney failure: acute renal failure occurred in 86 out of 2247 patients (3.8%) taking aspirin, and in 65 out of 972 patients (6.7%) not taking it [1]. This represented an approximate halving in the risk of acute renal failure.

Prof Sun said: "Thus, the results of this clinical study showed that pre-operative therapy with aspirin is associated with preventing about an extra three cases of acute renal failure per 100 patients undergoing CABG or/and valve surgery."

Acute renal failure or injury is a common post-operative complication and has a significant impact on the survival of patients undergoing heart surgery. "It significantly increases hospital stay, the incidence of other complications and mortality," said Prof Sun. "From previous reports, up to 30% of patients who undergo cardiac surgery develop acute renal failure. In our studies, about 16-40% of cardiac surgery patients developed it in various degrees, depending upon how their kidneys were functioning before the operation. Despite intensive studies we don't understand yet why kidney failure can develop after cardiac surgery, but possible mechanisms could involve inflammatory and neurohormonal factors, reduced blood supply, reperfusion injury, kidney toxicity and/or their combinations."

He continued: "For many years, aspirin as an anti-platelet and anti-inflammatory agent has been one of the major medicines in prevention and treatment of cardiovascular disease in non-surgical settings. Now its applications have spread to surgical fields, including cardiac surgery, and further, to non-cardiovascular diseases, such as the prevention of cancer. Looking back and ahead, I believe we can say that aspirin is really a wonder drug, and its wide applications and multiple benefits are truly beyond what we could expect and certainly worthy of further studies both in bench and bedside research."

Prof Sun said that more observational and randomised controlled clinical trials were required to investigate the role played by aspirin in preventing post-operative kidney failure, but he believed that the effect might also be seen in patients undergoing non-cardiac surgeries.

"For instance, the PeriOperative ISchemic Evaluation-2 trial (POISE-2) [2] is ongoing and aims to test whether small doses of aspirin, given individually for a short period before and after major non-cardiac surgeries, could prevent major cardiovascular complications such as heart attacks and death, around the time of surgery."

Other findings from Prof Sun's research showed that diabetes, high blood pressure, heart disease, heart failure, and diseases of the vascular system were all independent risk factors for post-operative acute kidney failure.

*Abstract no: 4AP6-8, Sunday 16.00 hrs (CEST).*

*[1] These figures are slightly different to those in the abstract as they have been updated since the abstract was submitted.*

*[2] Details of the POISE-2 trial can be found at: <http://clinicaltrials.gov/ct2/show/NCT01082874>*

*[3] This research received no funding.*

[http://www.eurekalert.org/pub\\_releases/2012-06/tlc-prf060612.php](http://www.eurekalert.org/pub_releases/2012-06/tlc-prf060612.php)

## **Positive results from first human clinical trials of a first-generation artificial pancreas system**

### ***System in development from Animas-JDRF partnership successfully detects highs and lows and automatically adjusts insulin delivery in clinical setting with no safety concerns***

WEST CHESTER, Pa. – Results from the first feasibility study of an advanced first-generation artificial pancreas system were presented today at the 72nd Annual American Diabetes Association Meeting in Philadelphia.

Findings from the study indicated that the Hypoglycemia-Hyperglycemia Minimizer (HHM) System was able to automatically predict a rise and fall in blood glucose and correspondingly increase and/or decrease insulin delivery safely. The HHM System included a continuous, subcutaneous insulin pump, a continuous glucose monitor (CGM) and special software used to predict changes in blood glucose. The study was conducted by Animas Corporation in collaboration with JDRF as part of an ongoing partnership to advance the development of a closed-loop artificial pancreas system for patients with Type 1 diabetes.

"The successful completion of this study using the HHM System in a human clinical trial setting is a significant step forward in the development of an advanced first-generation artificial pancreas system," said Dr. Henry Anhalt, Animas Chief Medical Officer and Medical Director of the Artificial Pancreas Program. "It lays the foundation for subsequent clinical trials, bringing us one step closer to making the dream of an artificial pancreas a reality for millions of people living with Type 1 diabetes."

In June 2011, Animas received Investigational Device Exemption (IDE) approval from the U.S. Food and Drug Administration (FDA) to proceed with human clinical feasibility studies for the development of a closed-loop artificial pancreas system. The company partnered with the JDRF in January 2010 to begin developing such an automated system to help people living with Type 1 diabetes better control their disease.

"We are encouraged by the results of the first human trials in this partnership with Animas," said Aaron Kowalski, Ph.D., Assistant Vice President of Research at JDRF. "An artificial pancreas system that can not only detect, but can predict high and low blood sugar levels and make automatic adjustments to insulin delivery

would be a major advance for people with Type 1 diabetes. Such a system could alleviate a huge burden of managing this disease."

#### About the Studies

The trial was a non-randomized, uncontrolled feasibility study of 13 participants with Type 1 diabetes at one trial site in the United States. The investigational Hypoglycemia-Hyperglycemia Minimizer (HHM) system was studied for approximately 24 hours for each study participant during periods of open and closed loop control via a model predictive control algorithm with a safety module run from a laptop platform. Insulin and food variables were manipulated throughout the study time period to challenge and assess the system.

The primary endpoint was to evaluate the ability of the algorithm to predict a rise and fall in glucose above or below set thresholds and to command the pump to increase, decrease, suspend and/or resume insulin infusion accordingly. The secondary endpoint was to understand the HHM system's ability to safely keep glucose levels within a target range and to provide guidance for future system development. The study also examined the relationship between CGM trends and the control model's algorithm for insulin delivery.

[http://www.eurekalert.org/pub\\_releases/2012-06/sri-srs060712.php](http://www.eurekalert.org/pub_releases/2012-06/sri-srs060712.php)

### **Scripps Research scientists develop new tools to unveil mystery of the 'glycome' Technique will help scientists understand how cells' common sugar molecules influence inflammation, cancer metastasis, and related conditions**

LA JOLLA, CA - Scientists at The Scripps Research Institute have developed chemical compounds that can make key modifications to common sugar molecules ("glycans"), which are found on the surface of all cells in our body. The new study presents powerful new tools for studying these molecules' function, for example in cell signaling and immunity, and for investigating new treatments for chronic inflammation, autoimmune diseases, cancer metastasis, and related conditions.

The new study, which appears online in Nature Chemical Biology on June 10, 2012, describes compounds that selectively block the attachment to the cell of two types of sugar building blocks, sialic acid and fucose, which are found at the tips of cell surface glycans and can be critical to cell function.

"We've developed the first compounds that can easily get into cells and selectively shut down the enzymes that decorate glycans with sialic acid or fucose," said Scripps Research Professor James C. Paulson, the senior author of the new report.

#### **One of the Least Understood Domains of Biology**

The "glycome"—the full set of sugar molecules in living things and even viruses—has been one of the least understood domains of biology. While the glycome encodes key information that regulates things such as cell trafficking events and cell signaling, this information has been relatively difficult to "decode."

Unlike proteins, which are relatively straightforward translations of genetic information, functional sugars have no clear counterparts or "templates" in the genome.

Their building blocks are simple, diet-derived sugar molecules, and their builders are a set of about 250 enzymes known broadly as glycosyltransferases. Characterizing these enzymes is essential to understanding the glycome. But one of the most basic tools of enzyme characterization—a specific enzyme inhibitor that can work in cell cultures and in lab animals—has been lacking for most glycosyltransferase families.

Three years ago, Cory Rillahan, a PhD candidate working in Paulson's laboratory, set out to find compounds that can specifically inhibit two important families of glycosyltransferases: the fucosyltransferases, which attach fucose groups, and the sialyltransferases, which attach sialic acids.

"They tend to be the most biologically relevant, because they attach these sugar units at the very tips of the glycan chains, which is where proteins on other cells bind to them," said Rillahan.

Rillahan began a quest by developing a screening technique that could be used to sift rapidly through chemical compound libraries to find strong inhibitors of these two enzyme families. This high-throughput screening technique was described last year in the journal *Angewandte Chemie*. But while Rillahan waited to get access to a larger compound library, he read of a more focused, rational-design strategy that Canadian researchers had used to devise inhibitors of a different glycosyltransferase.

#### **Using 'Imposter' Molecules**

Rillahan quickly adapted this broad strategy against sialyl- and fucosyltransferases in work described in the new study.

Normally an enzyme such as a fucosyltransferase grabs its payload—fucose, in this case—from a larger donor molecule, then attaches the small sugar to a glycan structure. Rillahan created fucose analogs, "impostor" molecules that can be readily taken up by this process, but then jam it.

When one of these fucose analogs gets into a cell, it is processed into a donor molecule and grabbed by a fucosyltransferase—but can't be attached to a glycan. Rillahan also designed sialic acid analogs that have the same spoofing effects against sialyltransferases.

These analogs act as traditional enzyme inhibitors in the sense that they bind to their enzyme targets and thereby block the enzymes from performing their normal function. But Rillahan found that his analogs have a second effect on their targeted enzyme pathways. They lead to an overabundance of unusable, analog-containing donor molecules in a cell; and that overabundance triggers a powerful feedback mechanism that dials down the production of new donor molecules—the only functional ones.

"The cell is fooled into thinking that it has enough of these donor molecules and doesn't need to make more," Rillahan said. With the combination of this shutoff signal and the analogs' physical blocking of enzymes, affected cells in the experiments soon lost nearly all the fucoses and sialic acids from their glycans.

### **Therapeutic Potential**

One important glycan that is normally decorated with fucoses and sialic acids is known as Sialyl Lewis X. It is highly expressed on activated white blood cells and helps them grab cell-adhesion molecules called selectins on the inner walls of blood vessels.

The velcro-like effect causes the circulating white blood cells to roll to a stop against the vessel wall, whereupon they exit the bloodstream and infiltrate local tissues. The overexpression of Sialyl Lewis X or the selectins that grab this structure has been linked to chronic inflammation conditions and various cancers.

Rillahan treated test cells with his best fucose and sialic acid analogs, and showed that virtually all the sialic acids and fucoses disappeared from Sialyl Lewis X molecules within a few days. Such cells were much less likely to roll to a stop on selectin-coated surfaces—suggesting that they would be much less likely to cause inflammation or cancer metastasis.

Paulson, Rillahan, and their colleagues now are working to reproduce the effects of these enzyme-inhibiting analogs in laboratory mice. "The idea is to show that these compounds can be effective in reducing the cell trafficking that contributes to inflammation and metastasis, but without harming the animals," Paulson said. The researchers also plan to use Rillahan's screening technique to sift through large compound libraries, to try to find compounds that inhibit specific enzymes within the sialyltransferase and fucosyltransferase families. Such enzyme-specific inhibitors might have narrower treatment effects and fewer side effects than broader, family-specific inhibitors.

In addition to Paulson and Rillahan, co-authors of the paper, "Global Metabolic Inhibitors of Sialyl- and Fucosyltransferases Remodel the Glycome," are Aristotelis Antonopoulos, Anne Dell, and Stuart M. Haslam of Imperial College, London, who performed mass-spectrometry analyses to confirm the absence of sialic acids and fucoses from treated cells; Roberto Sonon and Parastoo Azadi of the University of Georgia, whose tests demonstrated the feedback-shutdown of donor molecule synthesis in treated cells; and Craig T. Lefort and Klaus Ley of the La Jolla Institute for Allergy and Immunology, who performed the cell rolling tests.

*The research was funded in part by the National Institutes of Health.*

[http://www.eurekalert.org/pub\\_releases/2012-06/aaos-tro053112.php](http://www.eurekalert.org/pub_releases/2012-06/aaos-tro053112.php)

### **Top risk of stroke for normal-weight adults: Getting under 6 hours of sleep Stroke risk greatest for employed middle to older ages, normal weight and no sleep apnea, habitually sleeping less than 6 hours each day**

DARIEN, IL – Habitually sleeping less than six hours a night significantly increases the risk of stroke symptoms among middle-age to older adults who are of normal weight and at low risk for obstructive sleep apnea (OSA), according to a study of 5,666 people followed for up to three years.

The participants had no history of stroke, transient ischemic attack, stroke symptoms or high risk for OSA at the start of the study, being presented today at SLEEP 2012. Researchers from the University of Alabama at Birmingham recorded the first stroke symptoms, along with demographic information, stroke risk factors, depression symptoms and various health behaviors.

After adjusting for body-mass index (BMI), they found a strong association with daily sleep periods of less than six hours and a greater incidence of stroke symptoms for middle-age to older adults, even beyond other risk factors.

The study found no association between short sleep periods and stroke symptoms among overweight and obese participants. "In employed middle-aged to older adults, relatively free of major risk factors for stroke such as obesity and sleep-disordered breathing, short sleep duration may exact its own negative influence on stroke development," said lead author Megan Ruitter, PhD. "We speculate that short sleep duration is a precursor to

other traditional stroke risk factors, and once these traditional stroke risk factors are present, then perhaps they become stronger risk factors than sleep duration alone."

Further research may support the results, providing a strong argument for increasing physician and public awareness of the impact of sleep as a risk factor for stroke symptoms, especially among persons who appear to have few or no traditional risk factors for stroke, she said.

"Sleep and sleep-related behaviors are highly modifiable with cognitive-behavioral therapy approaches and/or pharmaceutical interventions," Ruitter said. "These results may serve as a preliminary basis for using sleep treatments to prevent the development of stroke."

Ruitter and colleagues collected their data as part of the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, led by George Howard, PhD, of the University of Alabama at Birmingham School of Public Health. REGARDS enrolled 30,239 people ages 45 and older between January 2003 and October 2007, and is continuing to follow them for health changes. The study is funded by the National Institutes of Health (NIH) National Institute of Neurological Disorders and Stroke.

*The abstract "Short sleep predicts stroke symptoms in persons of normal weight" is being presented today at SLEEP 2012, the 26th annual meeting of the Associated Professional Sleep Societies (APSS) in Boston. To be placed on the mailing list for SLEEP 2012 press releases or to register for SLEEP 2012 press credentials, contact AASM PR Coordinator Doug Dusik at 630-737-9700 ext. 9364, or at ddusik@aasmnet.org.*