

### **Cannabis linked to earlier onset of psychosis**

***A new study has provided the first conclusive evidence that cannabis use significantly hastens the onset of psychotic illnesses during the critical years of brain development – with possible life-long consequences.***

The first ever meta-analysis of more than 20,000 patients shows that smoking cannabis is associated with an earlier onset of psychotic illness by up to 2.7 years.

The analysis, by an international team including Dr Matthew Large, from the University of New South Wales (UNSW) School of Psychiatry and Sydney's Prince of Wales Hospital, is published today in the prestigious journal Archives of General Psychiatry.

In partnership with St Vincent's Hospital and The George Washington University School of Medicine and Health Sciences, the study set out to establish the extent to which use of cannabis, alcohol and other psychoactive substances affects the age at onset of psychotic illnesses such as schizophrenia.

Cannabis is the most widely used illicit drug in Australia with 33.5% of the population reporting use at some time, according to the 2007 National Drug Household Survey. Some 18% of all secondary school students aged 12-17 reported using the drug at some time in their life, according to the 2004 Secondary School Survey. (UNSW's National Cannabis Prevention and Information Centre <http://ncpic.org.au/>)

Building on several decades of research, the finding is an important breakthrough in the understanding of the relationship between cannabis use and psychosis, Dr Large said.

A number of previous studies have found an association between psychosis and the use of cannabis, alcohol and other psychoactive substances. However, the aim of this study was to specifically show the extent to which this is caused by cannabis use alone, he said.

The current findings support the view that cannabis use precipitates schizophrenia and other psychotic disorders, perhaps through an interaction between genetic and environmental disorders or by disrupting brain development, the team notes.

"The study re-analysed the results from 20,000 patients with schizophrenia or other psychotic illnesses from 83 previous studies. The study used meta-analysis – a modern statistical method – to show that an earlier onset of severe mental illness among substance users is a result of cannabis use, and cannot be explained by other factors such as alcohol use," Dr Large said.

"Results of this study are conclusive and clarify previously conflicting evidence of a relationship between cannabis use and the earlier onset of a psychotic illness, with evidence supporting the theory that cannabis use plays a causal role in the development of psychosis in some patients."

Dr Large said there was a high prevalence of substance use among individuals treated in mental health settings, and patients with schizophrenia were more likely to use substances than members of the wider community.

"The results of this study provide strong evidence that stopping or reducing cannabis use could delay or even prevent some cases of psychosis.

"The study raises the question of whether those substance users would still have gone on to develop psychosis a few years later.

"However, even if the onset of psychosis were inevitable, an extra two or three years of psychosis-free functioning could allow many patients to achieve important developmental milestones of late adolescence and early adulthood that could lower long-term disability arising from psychotic disorders," Dr Large said.

"The results of this study confirm the need for an ongoing public health warning about the potentially harmful effects of cannabis." *A high resolution video of this material is available:*

[http://www.youtube.com/watch?v=4JC-4EXzD9k&feature=player\\_embedded](http://www.youtube.com/watch?v=4JC-4EXzD9k&feature=player_embedded)

[http://www.eurekalert.org/pub\\_releases/2011-02/uorm-ttp020311.php](http://www.eurekalert.org/pub_releases/2011-02/uorm-ttp020311.php)

### **Therapy to prevent heart failure more effective in women than men**

***Never before has a therapy proven more beneficial for women than men in preventing heart disease – until now.***

A new study, published today in the Journal of the American College of Cardiology, found that women receive a significantly greater benefit – a 70 percent reduction in heart failure and a 72 percent reduction in death – from cardiac resynchronization therapy with defibrillator (CRT-D) than men.

"In prior cardiac studies, men and women generally received similar benefit from preventive medical therapy," said cardiologist Arthur J. Moss, M.D., professor of Medicine at the University of Rochester Medical Center and lead author of the study. "Our finding was unexpected, but extremely important because this is the only heart treatment that is clearly better in women than men."

Historically, heart disease has been dominated by its association with men. But, thanks to successful awareness campaigns in recent years, such as the American Heart Association's Go Red for Women initiative, women have started to take note of their risks and take action to protect their health.

On all fronts, women receiving CRT-D therapy to prevent heart failure progression had significantly better outcomes than men receiving the therapy. Reduction of heart failure in females was twice that of males – 70 percent versus 35 percent.

In women with mild heart failure, CRT-D therapy effectively prevented deterioration of the heart, otherwise known as cardiac remodeling, by preventing enlargement of the heart with more effective contraction of the heart.

Study authors investigated the reasons for the significantly better result in women than men. Women in the study were more likely to have non-ischemic heart disease, a disorder typically characterized by inflammatory scarring of the heart muscle, while men had a greater likelihood of ischemic heart disease – otherwise known as coronary artery disease – where narrowed arteries restrict the flow of blood and oxygen to the heart. Additionally, more women had left bundle branch block, a condition that results in disorganized electrical activity throughout the heart.

Because left bundle branch block and non-ischemic heart disease lead to diffuse, as opposed to localized, heart problems, study authors reasoned women were more responsive to CRT-D therapy, a treatment that strengthens the overall mechanical pumping action of the heart and coordinates the heart's electrical activity.

"It's not that men did poorly in the trial, but rather, women had really fantastic results, likely due to they type of heart disease we see more commonly in women," noted Moss.

The CRT-D device, developed by Boston Scientific, was originally approved to treat patients with severe heart failure. In September 2010, the Food and Drug Administration extended the approval of the Boston Scientific device to patients with mild heart failure to prevent progression to advanced heart failure. With the new indication, nearly 4 million more Americans are candidates for treatment with the CRT-D.

CRT-D therapy combines an implantable cardioverter defibrillator (ICD), which is designed to prevent sudden, rhythm-related cardiac death, with cardiac resynchronization therapy (CRT), which improves heart function with a reduction in heart failure and associated symptoms.

The study is a sub-analysis of the MADIT-CRT trial that was published in 2009 in the New England Journal of Medicine. The study involved 1,820 participants from 110 medical centers in the United States, Canada and Europe and compared the effectiveness of CRT-D versus ICD therapy in reducing heart failure and death during four and one-half years of follow-up. Twenty-five percent, or 453 of the study participants, were female.

Currently, 42 million American women are living with heart disease. It is the leading killer of women in the United States, each year claiming more women than men. In 2005, cardiovascular disease claimed the lives of more than 450,000 women, while all forms of cancer claimed the lives of approximately 265,000 women, according to the American Heart Association.

*The study was a joint effort between Boston Scientific and the University of Rochester Medical Center, with the participation of patients from medical centers throughout the world. Aysha Arshad, M.D., and Jonathan Steinberg, M.D., from St. Luke's and Roosevelt Hospitals and Columbia University College of Physicians and Surgeons in New York City are the major co-authors of the article. Moss holds no stock in any device company, has never been a member of any corporate speakers' bureau, and since Dec. 1, 2008, has chosen not to accept honoraria from Boston Scientific for any professional activity.*

[http://www.eurekalert.org/pub\\_releases/2011-02/ci-uer020711.php](http://www.eurekalert.org/pub_releases/2011-02/ci-uer020711.php)

### **Unexpected exoskeleton remnants found in Paleozoic fossils**

**Washington, D.C.—Surprising new research shows that, contrary to conventional belief, remains of chitin-protein complex—structural materials containing protein and polysaccharide—are present in abundance in fossils of arthropods from the Paleozoic era.**

Previously the oldest molecular signature of chitin-protein complex was discovered in 25 million year old Cenozoic fossils and remnants of structural protein have also been discovered in 80 million-year-old Mesozoic fossils. Carnegie's George Cody and an international team of scientists discovered relicts of protein-chitin complex in fossils of arthropods from the Paleozoic era. Their findings, published online by Geology, could have major implications for our understanding of the organic fossil record.

Among other common features, arthropods have exoskeletons, or cuticles. The outer portions of these cuticles are made up of a composite of chitin fibers, which are embedded in a matrix of protein. It is well known that chitin and structural protein are easily degraded by microorganisms and it has long been believed that chitin and structural proteins would not be present in fossils of moderate age, let alone in fossils dating back to the early Paleozoic.

Cody and his team studied fossil remains of a 310-million-year-old scorpion cuticle from northern Illinois and a 417-million-year-old eurypterid—an extinct scorpion-like arthropod, possibly related to horseshoe crabs—from Ontario, Canada. Using sophisticated analytical instrument at the Advanced Light Source facility, the research team measured the absorption spectra of low-energy X-rays by carbon, nitrogen, and oxygen in the fossils. These measurements were taken at a resolution on the order of 25 nanometers. The researchers showed that the majority of carbon, nitrogen and oxygen found in these fossils from the Paleozoic era were derived from a protein-chitin complex. Not surprisingly, the protein-chitin material was somewhat degraded, either by chemical processes or partial bacterial degradation.

Cody speculates that the vestigial protein-chitin complex may play a critical role in organic fossil preservation by providing a substrate protected from total degradation by a coating waxy substances that protect the arthropods from desiccation.

*This research was supported by funds from National Aeronautics and Space Administration Astrobiology Institute and Massachusetts Institute of Technology. Some of the researchers were supported by donations to the American Chemical Society Petroleum Research Fund. The analyses reported here were performed at the Advanced Light Source at Lawrence Berkeley Laboratory—a Department of Energy supported facility.*

[http://www.eurekalert.org/pub\\_releases/2011-02/w-lrt020711.php](http://www.eurekalert.org/pub_releases/2011-02/w-lrt020711.php)

### **Less radical tumor surgery can offer better long-term kidney function**

***Patients with kidney tumours larger than four centimetres are much more likely to enjoy good long-term renal function if they undergo nephron-sparing surgery rather than radical nephrectomy, according to a study in the February issue of the urology journal BJUI.***

Researchers from the Department of Urology at Johannes Gutenberg University in Mainz, Germany, studied 166 patients for up 19 years, with a median follow up of five-and-a-half years. The participants were split into two groups - 81 "younger" patients up to 55 and 85 "older" patients aged 65 and over.

They found that, regardless of age, the patients who underwent radical nephrectomy (RN) were twice as likely to develop new onsets of chronic kidney disease than those who underwent nephron-sparing surgery (NSS).

"In RN the surgeon removes the whole kidney and the tissue around it, while in NSS the surgeon removes the cancer and part of the kidney surrounding it so that the patient still has some working kidney left after the operation" explains lead researcher Dr Frederik C Roos.

"Overall survival and complication rates were similar between the two groups, but long-term kidney function, which is very important to overall health and quality of life, was much better in the patients who had received NSS.

"Kidney tumours are more common in people in their 60s and 70s and increasing life expectancy means that more elderly patients will seek treatment for this condition.

"Our results show that 76% of older patients enjoyed good long-term kidney health with NSS as did 85% of younger patients.

"This is important as loss of kidney function is also associated with other health issues, including higher incidence of cardiovascular disease and cardiac deaths and reduced function in other organs."

Key findings included:

\* The incidence of chronic kidney disease in younger patients (aged 23 to 55) was 31% after RN and 16% after NSS. In older patients (aged 65 to 84) it was 51% and 24% respectively.

\* Overall survival (OS) rates did not differ significantly between surgical procedures. In the younger age group, the OS rates for NSS and RN patients were 92% and 91% at five years and 84% and 70% at 15 years. In the older group - where death from any cause was included - they were 72% and 89% at five years and 18% and 41% at 15 years.

\* Complication rates were similar for both procedures, occurring in 35% of younger patients and 26% of older patients. They occurred in 16 NSS and 12 RN patients in the younger group and 10 NSS and 11 RN patients in the older group. There were no deaths as a result of the surgery.

"It is important to choose the type of surgery that patients receive for kidney tumours based on a number of factors, such as tumour features, biological age, other illnesses and the patient's wishes and social support" says Dr Roos. "The patient's actual age should not be a factor in whether they receive the surgery.

"We believe that our research shows that, if the factors we have outlined above make NSS feasible, it is the best surgical option for younger patients and carefully selected older patients with a kidney tumour of four centimetres or more."

*Notes to editors Perioperative morbidity and renal function in young and elderly patients undergoing elective nephron-sparing surgery or radical nephrectomy for renal tumours larger than 4cm. Roos at al. BJUI. 107, pp554-561 (February 2011). DOI: 10.1111/j.1464-410X.2010.09516.x*

## Without language, numbers make no sense

\* 20:00 07 February 2011 by Bob Holmes

**People need language to fully understand numbers. This discovery – long suspected, and now backed by strong evidence – may shed light on the way children acquire their number sense.**

Previous studies of Amazon tribes who lack words for numbers greater than three – or, in the case of the Pirahã, for any numbers at all – had shown that they struggle to understand precise quantities, when numbers are relatively large.

However, it wasn't clear whether this is because they lacked words for larger numbers, or because they came from a culture that viewed precise numbers as unimportant.

Now Elizabet Spaepen, a psychologist at the University of Chicago, and her colleagues may have settled the question. The team studied profoundly deaf people from Nicaragua who had created their own sign language to communicate.

### Wordless numbers

These "homesigners" live in a numerate culture, holding jobs and using money, yet lack any vocabulary for numbers. So the researchers reasoned that any difference in their numeracy must be down to language alone.

Spaepen's team tested their number sense by asking four homesigning adults to summarise picture stories in which numbers played an important part, for example a story featuring 10 sheep in a pen. Spanish-speaking Nicaraguans who weren't deaf and deaf people who used American Sign Language performed these tasks almost flawlessly.

In contrast, homesigners were only accurate at counting the smallest numbers. Beyond three or four they were often imprecise, for example holding out nine fingers to represent 10 sheep.

In a further task, homesigners were given a set of objects and asked to use tokens to create a second set containing the same number of tokens as objects. Again, their accuracy dropped significantly above sets of three objects.

"They're not wildly off," says Spaepen. "They can approximate quantities, but they don't have a way of getting to the exact number."

### Count list

Spaepen's experiments did not reveal which component of language is crucial to developing an accurate number sense. However, she suspects that it is the "count list" – the familiar sequence of numbers that every speaking child learns early on.

Children learn this count list well before they actually understand that "four" refers to four objects rather than three or six, says Michael Frank at Stanford University in California.

*Journal reference: Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.1015975108*

<http://www.bbc.co.uk/news/health-12265572>

## Sleepwalking 'linked to chromosome fault'

By Michelle Roberts Health reporter, BBC News

**Scientists believe they have discovered the genetic code that makes some people sleepwalk.**

By studying four generations of a family of sleepwalkers they traced the fault to a section of chromosome 20.

Carrying even one copy of the defective DNA is enough to cause sleepwalking, the experts told the journal *Neurology*.

They hope to target the genes involved and find new treatments for the condition that affects up to 10% of children and one in 50 adults.

Most often, sleepwalking is a fairly benign problem and something that will be outgrown.

Many children will have episodes where they will arise from their sleep in a trance-like state and wander.

But more extreme cases of sleepwalking can be deeply disruptive and downright dangerous, particularly when the condition persists into adulthood.

### Stress trigger

Sleepwalkers may perform complex feats such as locating the car keys, unlocking the doors and then driving.

There have even been high-profile cases where sleepwalkers have killed during an episode.

Despite this relatively little is known about the phenomenon, called somnambulism by medics.

### Sleepwalking

\* Happens during deep non-dreaming sleep, typically not long after the person has fallen asleep



\* Episodes can range from a person simply sitting up in bed, to walking around, getting dressed and leaving the house

\* Is most common in children but can persist into adulthood

\* Episodes usually last a few minutes

\* It can be difficult to wake a sleepwalker and, usually, they will return to bed of their own accord

Experts do know that sleepwalking tends to run in families and that some people are particularly susceptible to it.

And factors like being over-tired or stressed can be the trigger.

Typically, episodes happen early in the night, soon after the individual has fallen asleep and is in the deep, dreamless "slow wave" or non-rapid eye movement (NREM) stage of sleep.

By morning, the person will usually have no recollection of the episode.

For the latest study, Dr Christina Gurnett and colleagues at the Washington University School of Medicine sought the help of a large family of sleepwalkers.

The family had been referred to them because one of the youngest members, a 12-year-old girl called Hannah, had been experiencing particularly troublesome sleepwalking, which regularly caused her to leave the house and roam during the night.

Among the four generations of the family, spanning from the great-grandparents downwards, nine members out of the 22 were sleepwalkers.

One family member - an uncle of Hannah's - frequently wakes to find he has put on eight pairs of socks during the night. Some of her other sleepwalking relatives have suffered injuries such as broken toes during their nocturnal wanderings.

Using saliva samples the researchers analysed the family's DNA to unpick the genetics of the condition.

A genome-wide search revealed the problem stemmed from genetic code housed on chromosome 20, and that this code had been passed down from generation to generation. Someone with the gene has a 50% chance of passing it on to their children.

And any individual who inherited a copy of the faulty DNA would be a sleepwalker, they found.

Although they have yet to identify the precise gene or genes involved - there are a potential 28 - their hunch is that it will be the adenosine deaminase gene that is the culprit.

This gene, which sits in the minute segment of chromosome 20 that the researchers identified, is already known to be linked to the slow wave sleep that sleepwalking occurs within.

Child's feet Sleepwalking is more common during childhood

Dr Gurnett said: "It is likely that several genes will be involved. What we have found is the first genetic locus for sleepwalking.

"We do not know yet which of the genes in this linkage region of chromosome 20 will be responsible. Until we find the gene we won't know whether this accounts for several families or a large number of families who have sleepwalking.

"But discovering these genes could help with identifying and treating the condition."

Dr Malcolm von Schantz, a sleep expert at the University of Surrey, said: "This provides the proof of concept. We are beyond the needle in the haystack stage. It's now become feasible to find out which mutation in which gene is responsible."

<http://www.nytimes.com/2011/02/08/science/08obpolynesia.html>

## **DNA Sheds New Light on Polynesian Migration**

**By SINDYA N. BHANOO**

### ***New genetic research reveals that the migratory story of the Polynesians may be more ancient and complicated than previously thought.***

For years, it was generally accepted that Polynesians originated in modern-day Taiwan and began moving south and east about 4,000 years ago. This migration account is based on the research of linguists, the findings of archeologists and some genetic analysis.

But a new study in The American Journal of Human Genetics reports that Polynesians began migrating thousands of years earlier, not from Taiwan, but from mainland Southeast Asia.

The study looked at mitochondrial DNA, which gives information about maternal ancestry. The researchers compared DNA samples from more than 4,700 people in Southeast Asia and Polynesia.

Based on this, they determined that Polynesians arrived in the Bismarck Archipelago of Papua New Guinea at least 6,000 to 8,000 years ago, via Indonesia, and presumably left the mainland about 10,000 years ago.

Linguists believe that Polynesian languages belong to the Austronesian language family, which originated in Taiwan.

Though the new research seems to leave the linguists in the lurch, Martin Richards, an archaeogeneticist at the University of Leeds in Britain and one of the study's authors, believes there might be a reasonable explanation.

"It's still possible there was the elite movement from Taiwan much later that transferred the language," he said. "The idea would be that we do have very minor lineages that look like they came to Bismarck about 3,500 years ago and may have caused a language shift."

The original migration from the mainland may have had to do with natural climate change.

"They may have just ended up there because of sea level rises occurring at the time, and the formation of an archipelago," Dr. Richards said.

[http://www.eurekalert.org/pub\\_releases/2011-02/wuso-gpl020811.php](http://www.eurekalert.org/pub_releases/2011-02/wuso-gpl020811.php)

**Gene protects lung from damage due to pneumonia, sepsis, trauma, transplants**  
**Lung injury is a common cause of death among patients with pneumonia, sepsis or trauma and in those who have had lung transplants.**

The damage often occurs suddenly and can cause life-threatening breathing problems and rapid lung failure.

There are no effective treatments. Patients usually are put on ventilators to give their lungs a chance to heal, but there is little else doctors can do but wait and hope for the best.

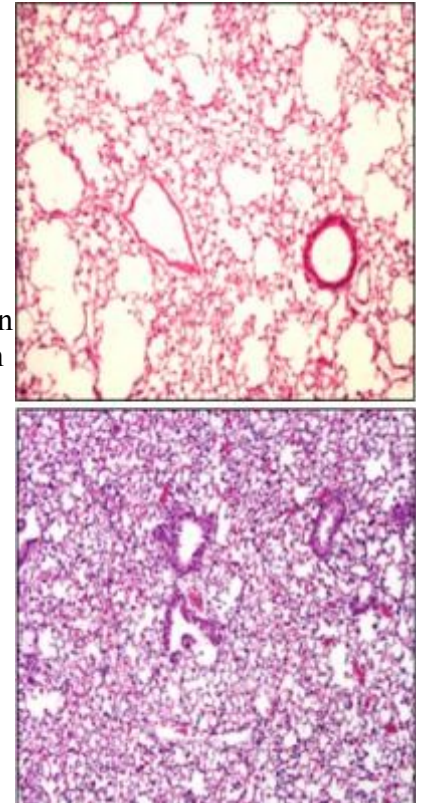
Now, researchers at Washington University School of Medicine in St. Louis report they have identified a gene that limits damage to the lung during acute stress from illness, trauma or transplant. Defects in the *bcl3* gene likely leave some patients more vulnerable to lung injury, they say.

The scientists also have demonstrated that this critical gene, which is active in bone marrow cells, can prevent lung injury in mice. The research is published in the *Journal of Clinical Investigation*.

The new discovery lays the groundwork for developing therapies to reduce complications of pneumonia, trauma and lung transplants, which affect many thousands of people annually in the United States.

"Acute lung injury is a very serious problem," says senior author Andrew Gelman, PhD, assistant professor of surgery and of pathology and immunology. "Patients' lungs fill with fluid, they can't breathe, and sadly there are no drugs available to reverse the condition."

The real culprits underlying acute lung injury are infection-fighting white blood cells called neutrophils. When the body makes too many neutrophils, however, they begin to attack healthy tissue, causing even more damage and sometimes even death.



**Top, a healthy transplanted lung in a normal mouse. Below, a severely injured lung, damaged after transplant, in a mouse lacking the *bcl3* gene in bone marrow. The damage is caused by the overproduction of neutrophils, which attack healthy tissues. Andrew Gelman**

"In mice, we found that the *bcl3* gene essentially controls how many neutrophils the body produces under acute stress in the lung," Gelman says.

The same gene exists in people. Mutations in *bcl3* have long been associated with the development of leukemia and lymphoma. Only recently has it been found to play a role in inflammation.

The research team stumbled onto *bcl3* as part of an effort to determine why a newly transplanted lung often becomes injured in the hours after surgery. The damage occurs as the blood begins to flow through the organ again and increases the risk of rejection. In earlier studies, they had found that soon after a lung transplant, the new lung signals to the bone marrow to produce massive amounts of neutrophils.

"We wanted to understand how the lung is talking to the bone marrow and what is driving this extraordinary increase in neutrophils," Gelman says. "The lung tends to be unique in this manner; we don't see this with other organ transplants, such as the heart."

In a series of experiments in mice undergoing lung transplants, the researchers found that in response to acute stress in the lung, a cytokine called granulocyte colony stimulating factor (G-CSF) accumulates in the blood, which in turn stimulates the production of neutrophils in the bone marrow.

But there's a counterbalance built into the system. When G-CSF builds up in the blood, the *bcl3* gene is activated in the bone marrow to begin shutting down neutrophil production.

When the scientists transplanted healthy mouse lungs into mice that lacked bcl3 in their bone marrow, things went haywire. Without the gene, neutrophil production went unchecked, and the mice developed acute lung injury.

The investigators measured four times as many neutrophils in the blood of mice that lacked bcl3 compared with normal mice. The bcl3 gene, they showed, acts like a master switch to control the effects of G-CSF on neutrophil production. While neutrophils are the key offenders of acute lung injury, completely blocking them from entering the lung is not a practical treatment.

"You need enough neutrophils in the lung to fight infection or repair lung damage but when there are too many, they cause irreversible injury," Gelman says. "It's a delicate balancing act."

Instead, the investigators showed they could prevent post-transplant lung injury by blocking G-CSF in mice that lacked bcl3 in their bone marrow.

"This reduced the number of neutrophils that entered the lung," Gelman explains. "Other inflammatory cytokines, including GM-CSF and IL-3, still produced neutrophils but not enough to cause acute lung injury."

The researchers also showed they could prevent acute lung injury in a mouse model of sepsis by blocking G-CSF in mice that lacked bcl3. Interestingly, G-CSF is routinely given to cancer patients undergoing chemotherapy to help them fight infections.

"There's been a lot of effort to stimulate neutrophil production in cancer patients because chemotherapy kills cancer cells and prevents the production of white blood cells, including neutrophils," Gelman says. "But what we're saying is that under acute stress to the lung, the effect of G-CSF on neutrophil production needs to be limited but certainly not eliminated."

In follow-up studies, Gelman and his colleagues want to get a better handle on how mutations in the bcl3 gene affect a person's susceptibility to acute lung injury from an infection or a transplant, he says.

*The research was funded by a grant from the National Heart, Lung, and Blood Institute.*

*Kreisel D, Sugimoto S, Tietjens J, Zhu J, Yamamoto S, Krupnick AS, Carmody RJ, Gelman AE. Bcl3 prevents acute inflammatory lung injury by restraining emergency granulopoiesis. Journal of Clinical Investigation. January 2011.*

[http://www.eurekalert.org/pub\\_releases/2011-02/uoia-bdv020811.php](http://www.eurekalert.org/pub_releases/2011-02/uoia-bdv020811.php)

### **Brief diversions vastly improve focus, researchers find**

**CHAMPAIGN, Ill. — A new study in the journal *Cognition* overturns a decades-old theory about the nature of attention and demonstrates that even brief diversions from a task can dramatically improve one's ability to focus on that task for prolonged periods.**

The study zeroes in on a phenomenon known to anyone who's ever had trouble doing the same task for a long time: After a while, you begin to lose your focus and your performance on the task declines.

Some researchers believe that this "vigilance decrement," as they describe it, is the result of a drop in one's "attentional resources," said University of Illinois psychology professor Alejandro Lleras, who led the new study. "For 40 or 50 years, most papers published on the vigilance decrement treated attention as a limited resource that would get used up over time, and I believe that to be wrong. You start performing poorly on a task because you've stopped paying attention to it," he said. "But you are always paying attention to something. Attention is not the problem."

Lleras had noticed that a similar phenomenon occurs in sensory perception: The brain gradually stops registering a sight, sound or feeling if that stimulus remains constant over time. For example, most people are not aware of the sensation of clothing touching their skin. The body becomes "habituated" to the feeling and the stimulus no longer registers in any meaningful way in the brain.

In previous studies, Lleras explored the limits of visual perception over time, focusing on a phenomenon called Troxler Fading: when continual attention to a stationary object in one's peripheral vision can lead to that object's complete "disappearance" from view.

"Constant stimulation is registered by our brains as unimportant, to the point that the brain erases it from our awareness," Lleras said. "So I thought, well, if there's some kind of analogy about the ways the brain fundamentally processes information, things that are true for sensations ought to be true for thoughts. If sustained attention to a sensation makes that sensation vanish from our awareness, sustained attention to a thought should also lead to that thought's disappearance from our mind!"

In the new study, Lleras and postdoctoral fellow Atsunori Ariga tested participants' ability to focus on a repetitive computerized task for about an hour under various conditions. The 84 study subjects were divided into four groups:

\* The control group performed the 50-minute task without breaks or diversions.

\* The "switch" group and the "no-switch" group memorized four digits prior to performing the task, and were told to respond if they saw one of the digits on the screen during the task. Only the switch group was



actually presented with the digits (twice) during the 50-minute experiment. Both groups were tested on their memory of the digits at the end of the task.

\* The "digit-ignored" group was shown the same digits presented to the switch group during the task, but was told to ignore them.

As expected, most participants' performance declined significantly over the course of the task. But most critically, Lleras said, those in the switch group saw no drop in their performance over time. Simply having them take two brief breaks from their main task (to respond to the digits) allowed them to stay focused during the entire experiment. "It was amazing that performance seemed to be unimpaired by time, while for the other groups performance was so clearly dropping off," Lleras said.

This study is consistent with the idea that the brain is built to detect and respond to change, Lleras said, and suggests that prolonged attention to a single task actually hinders performance.

"We propose that deactivating and reactivating your goals allows you to stay focused," he said. "From a practical standpoint, our research suggests that, when faced with long tasks (such as studying before a final exam or doing your taxes), it is best to impose brief breaks on yourself. Brief mental breaks will actually help you stay focused on your task!"

*Lleras is a researcher at the university's Beckman Institute for Advanced Science and Technology.*

*The paper, "Brief and Rare Mental 'Breaks' Keep You Focused: Deactivation and Reactivation of Task Goals Pre-empt Vigilance Decrements," is available from the News Bureau.*

[http://www.eurekalert.org/pub\\_releases/2011-02/wios-hfs020811.php](http://www.eurekalert.org/pub_releases/2011-02/wios-hfs020811.php)

### **Hope for stroke victims**

#### **2 new studies support a novel approach based on Weizmann Institute scientists' research**

Much of the devastation of stroke and head trauma is due to damage caused the overproduction of a substance in the brain called glutamate. Preventing this damage has been impossible, until now, as many drugs don't cross the so-called blood-brain barrier, and those that do often don't work as intended. But a method originally devised at the Weizmann Institute of Science may, in the future, offer a way to avert such glutamate-induced harm.

Prof. Vivian I. Teichberg of the Institute's Neurobiology Department first demonstrated a possible way around these problems in 2003. Glutamate – a short-lived neurotransmitter – is normally all but absent in brain fluids. After a stroke or injury, however, the glutamate levels in brain fluid become a flood that over-excites the cells in its path and kills them. Instead of attempting to get drugs into the brain, Teichberg had the idea that one might be able to transport glutamate from the brain to the blood using the tiny "pumps," or transporters, on the capillaries that work on differences in glutamate concentration between the two sides. Decreasing glutamate levels in blood would create a stronger impetus to pump the substance out of the brain. He thought that a naturally-occurring enzyme called glutamate-oxaloacetate transaminase (GOT, for short) could "scavenge" blood glutamate, significantly lowering its levels. By 2007, Teichberg and his colleagues had provided clear evidence of the very strong brain neuroprotection that oxolacetate (a chemical similar to GOT) afforded rats exposed to a head trauma.

Two new studies – conducted by Fransisco Campos and others from the lab of Prof. Jose Castillo in the University of Santiago de Compostela, Spain – now provide a definitive demonstration of Teichberg's results. In the first, the scientists conclusively showed that oxoloacetate injected into rats with stroke-like brain injuries reduces glutamate levels both in the blood and in the affected brain region, while significantly lessening both cell death and the swelling that can accompany stroke. In the second, a team of neurologists in two different hospitals checked the levels of glutamate and GOT in several hundred stroke victims who were admitted to their hospitals. They found that the most significant predictor of the prognosis – how well they would recover at three months and how much brain damage they would suffer – was the levels of these two substances. High glutamate levels correlated with a poor outcome, high GOT levels with a better one.

The overall implication of these two papers is that administering GOT might improve a patient's chances of recovering, as well as speeding up the process. In addition to stroke and head trauma, a number of diseases are characterized by an accumulation of glutamate in the brain, including Alzheimer's disease, Parkinson, multiple sclerosis, epilepsy, glaucoma, certain brain tumors and amyotrophic lateral sclerosis, and there is hope that, in the future, treatments to scavenge glutamate could relieve the symptoms and improve the outcomes for a number of neurological problems. Yeda, the technology transfer arm of the Weizmann Institute, holds a patent for this method.

*Prof. Vivian I. Teichberg's research is supported by the Nella and Leon Benoziyo Center for Neurosciences; the Carl and Micaela Einhorn-Dominic Brain Research Institute; and the Legacy Heritage Fund Program of the Israel Science Foundation. Prof. Teichberg is the incumbent of the Louis and Florence Katz-Cohen Professorial Chair of Neuropharmacology.*



## Eggs are now naturally lower in cholesterol

### **New study shows large eggs are 14 percent lower in cholesterol and 64 percent higher in vitamin D**

Park Ridge, IL – According to new nutrition data from the United States Department of Agriculture's Agricultural Research Service (USDA-ARS), eggs are lower in cholesterol than previously thought. The USDA-ARS recently reviewed the nutrient composition of standard large eggs, and results show the average amount of cholesterol in one large egg is 185 mg, 14 percent lower than previously recorded. The analysis also revealed that large eggs now contain 41 IU of vitamin D, an increase of 64 percent.

"We collected a random sample of regular large shell eggs from 12 locations across the country to analyze the nutrient content of eggs," says Dr. Jacob Exler, Nutritionist with the Agricultural Research Service's Nutrient Data Laboratory. "This testing procedure was last completed with eggs in 2002, and while most nutrients remained similar to those values, cholesterol decreased by 14 percent and vitamin D increased by 64 percent from 2002 values."

The collected eggs were sent to a laboratory at Virginia Tech University to be prepared for nutrient analysis at certified nutrient analysis laboratories. The samples were randomly paired for the testing procedure, and the analysis laboratories tested samples to determine composition of a variety of nutrients including protein, fat, vitamins and minerals. Accuracy and precision were monitored using quality control samples.

According to Dr. Exler, this procedure is standard for the National Food and Nutrient Analysis Program (NFNAP), the program responsible for analyzing the nutrient composition of a wide variety of foods and making nutrition information publicly available. This information is available on the nutrient data lab website at [www.ars.usda.gov/nutrientdata](http://www.ars.usda.gov/nutrientdata). The new nutrient information will also be updated on nutrition labels to reflect these changes wherever eggs are sold, from egg cartons in supermarkets to school and restaurant menus.

#### **Cracking Egg Myths**

Over the years, Americans have unnecessarily shied away from eggs – despite their taste, value, convenience and nutrition – for fear of dietary cholesterol. However, more than 40 years of research have demonstrated that healthy adults can enjoy eggs without significantly impacting their risk of heart disease.

"My research focuses on ways to optimize diet quality, and I have long suspected that eliminating eggs from the diet generally has the opposite effect. In our own studies of egg intake, we have seen no harmful effects, even in people with high blood cholesterol," says Dr. David Katz, Director of the Yale University Prevention Research Center.

Enjoying an egg a day can fall within current cholesterol guidelines, particularly if individuals opt for low-cholesterol foods throughout the day. The 2010 Dietary Guidelines for Americans suggest that eating one whole egg per day does not result in increased blood cholesterol levels and recommend that individuals consume, on average, less than 300 mg of cholesterol per day. A single large egg contains 185 mg cholesterol.

Some researchers believe the natural decrease in the cholesterol level of eggs could be related to the improvements farmers have made to the hens' feed. Hens are fed a high-quality, nutritionally balanced diet of feed made up mostly of corn, soybean meal, vitamins and minerals. Poultry nutrition specialists analyze the feed to ensure that the natural nutrients hens need to stay healthy are included in their diets. Nutrition researchers at Iowa State University are compiling a report to outline potential reasons for the natural decrease in cholesterol in eggs.

#### **Nutrient-Rich Eggs**

Eggs now contain 41 IU of vitamin D, which is an increase of 64 percent from 2002. Eggs are one of the few foods that are a naturally good source of vitamin D, meaning that one egg provides at least 10 percent of the Recommended Daily Allowance (RDA). Vitamin D plays an important role in calcium absorption, helping to form and maintain strong bones.

The amount of protein in one large egg – 6 grams of protein or 12 percent of the Recommended Daily Value – remains the same, and the protein in eggs is one of the highest quality proteins found in any food. Eggs are all-natural, and one egg has lots of vitamins and minerals all for 70 calories. The nutrients in eggs can play a role in weight management, muscle strength, healthy pregnancy, brain function, eye health and more. At less than 15 cents apiece, eggs are an affordable and delicious breakfast option.

*For more information on cholesterol and the nutritional benefits of eggs, along with recipes and cooking tips, visit [www.incredibleegg.org](http://www.incredibleegg.org).*

## Paper archives reveal pollution's history

***Some of the history preserved in old tomes and newspapers may be hiding in between the lines of print.***

A Weizmann Institute scientist has found that the paper in such collections contains a record of atmospheric conditions at the time the trees that went into making it were growing. By analyzing the carbon isotopes in bits of paper clipped from old magazines, Prof. Dan Yakir of the Environmental Sciences and Energy Research Department in the Faculty of Chemistry has traced the rising effects of atmospheric pollution from burning fossil fuel going back to beginnings of the industrial revolution.

Scientists generally reconstruct the record of past climate change from such sources as ice cores or tree rings. But a reliable tree ring history, says Yakir, requires an analysis of quite a few trees. "Rather than going to forests all over the world to sample trees," says Yakir, "we went to the local library." In the Weizmann library's archives, Yakir found issues of the scientific journals *Science*, *Nature* and the *Journal of the Royal Chemical Society* going back over 100 years to the late 19th century. Removing small samples from the margins of successive volumes, he took them back to the lab for analysis.

The analysis was based on a finding that the proportion of a carbon isotope – carbon 13 (13C) – to its lighter counterpart – carbon 12 (12C) – could provide information on the CO<sub>2</sub> added to the atmosphere from burning fossil fuel. This is based on a cycle that begins with plants taking up CO<sub>2</sub> in photosynthesis. All plants prefer to use CO<sub>2</sub> made with the more common version of carbon, 12C, than the slightly heavier 13C. Plant biomass from millions of years ago was transformed into reservoirs of oil, gas and coal, and so these are naturally low in 13C, as well. When we started to burn those reservoirs following the industrial revolution, we began returning the 13C-poor CO<sub>2</sub> to the atmosphere.

Now the atmospheric 13C content has become increasingly diluted, and this is reflected in the carbon ratios in the trees milled for pulp and paper. Yakir's work shows that this continuing dilution is, indeed, clearly recorded in the archival paper and, plotted over time, it demonstrates the increasing intensity of our fossil fuel burning in the past 150 years.

This project has been ongoing for about 14 years, with figures from new issues added over time. In the process, says Yakir, he has had to learn something about the paper industry. Some early issues, for instance, had been printed on rag paper (made of cotton, flax, etc.) rather than wood pulp, while blips in the data around the time of WWII led Yakir to suspect that the paper was either recycled, or again supplemented with rag content to make up for wartime shortages.

Anomalies aside, 13C levels in the paper, especially for two of the journals, were a good match for existing atmospheric records, and even revealed some local phenomena, including differences between American and European records. In addition to alerting climate scientists to a very well organized, untapped, source of global change records, says Yakir, the technique could be used to authenticate antique paper samples.

*Prof. Dan Yakir's research is supported by the Cathy Wills and Robert Lewis Program in Environmental Science and the estate of Sanford Kaplan.*

<http://www.nytimes.com/2011/02/08/health/research/08disparities.html>

## **Disparities: A Growing Gender Gap in Doctors' Pay**

**By RONI CARYN RABIN**

***Starting salaries for women who become physicians are significantly lower than men's, and the pay gap has grown over the past decade, a study reports.***

The pay differential, which was 12.5 percent in 1999, increased to nearly 17 percent by 2008, according to the report, published Thursday in *Health Affairs*.

The growing gap could not be explained by women's preferences, the authors said. While women on average do choose lower-paying specialties and shorter workweeks than men, those disparities were less pronounced in 2008 than in 1999. Yet the pay differential has widened.

"That was the part that surprised and puzzled us," said one author, Anthony T. Lo Sasso, a professor of health policy at the University of Illinois at Chicago. "As you start moving forward in time closer to the present day, your ability to explain away that difference between men's and women's salaries essentially evaporates."

The research looked at more than 8,000 new physicians in New York State. In 1999, the women earned \$151,600 on average, compared with \$173,400 for men; by 2008, the figures were \$174,000 for women and \$209,300 for men. (The study adjusted for inflation.) After accounting for differences in their practices, the study concluded, the pay gap had increased to \$16,819 in 2008, from \$3,600 in 1999.

## **Personality disorders are 'widespread', say experts**

***We need to be more aware of personality disorders - which are more prevalent than people realise, say experts.***

Prof Eddie Kane, of the Institute of Mental Health, said 4% of people have such a condition, with some studies showing rates as high as 13%. These vary in severity and in personality disorder type.

People with personality disorders are more likely to end up in prison, commit suicide and have mental health problems. A personality disorder is defined as a pattern of behaviour that deviates markedly from the individual's culture.

Those with personality disorders repeatedly behave in a way that is not acceptable to the community that they live in and cause distress to themselves, or others.

There is a range of different disorders including borderline, anti-social, paranoid and narcissistic.

Doctors say that one of the reasons they are so difficult to treat is that the disorder is ingrained in a person's behaviour - in the same way that we all have ingrained personality traits.

Dr Kingsley Norton, personality disorder lead at West London Mental Health Trust, said: "We all have personalities and it is difficult for us to change the way we behave if it goes against our personality 'type'.

"For example, a belief that people with personality disorders often have is, 'people cannot be trusted - they will always let you down.'

"This is a core belief to that person and will govern the way that they interact with everybody."

That can lead to unco-operative behaviour that is threatening or aggressive - and can get the person with the disorder into trouble.

### **Personality Disorder types and the associated symptoms**

- \* Odd/Eccentric: people can be paranoid; indifferent to social relationships; unable to relate to people; have an unusual appearance
- \* Dramatic: people can be histrionic; narcissistic; have unstable moods; fear being abandoned and self-harm.
- \* Anxious: people can be preoccupied with orderliness and perfectionism. They may fear negative evaluation; feel inadequate in social situations; are dependent and submissive.

Most people with personality disorders do not commit offences.

However, for some it significantly contributes to behaviour that gets them involved in the criminal justice system. About two-thirds of prisoners meet the criteria for at least one type of personality disorder and they have a higher risk of drug abuse.

### **Staff training**

Leading experts say the disorders are under recognised - even though the numbers of people suffering from personality disorders is much higher than those with more well known problems, such as schizophrenia.

Prof Kane, director of the Personality Disorder Institute at the Institute of Mental Health, University of Nottingham, said: "Although 4% is the generally accepted figures for prevalence some international studies have shown prevalence as high as 13%.

"But because personality disorder is not a disease it does not attract the sympathy that conditions such as schizophrenia does."

Experts are now trying to train those who are most likely to come into contact with a personality disorder how to recognise the condition to make the situation easier to manage.

This is crucial because the way in which staff interact with someone who has a personality disorder can affect the patient's condition.

Dr Norton said: "If the relationship with a patient is not right, it will affect the condition adversely but relationships can also be a cure. It is therefore very important that staff are trained properly."

Prof Kane has developed a training programme for staff that are most likely to come into contact with those who have personality disorders.

It uses video reconstructions to show the types of situations where staff may encounter someone with a personality disorder and what they can do to keep the situation in control.

So far, the programme has been rolled out to a variety of staff including prison officers, police officers, GP receptionists and nurses. About 5,000 people will have been trained by 2012. In the future professionals working in education and with younger people are likely to get training.

Prof Kane said it could stop difficult situations escalating: "This training helps people to understand personality disorders.

"It is delivered by a trainer and a person with a personality disorder. Feedback from those with personality disorders has shown that it makes a big difference to their experiences in those situations."

## **New hybrid drug, derived from common spice, may protect, rebuild brain cells after stroke**

### **Study from Cedars-Sinai Medical Center presented at American Heart Association International Stroke Conference**

Whether or not you're fond of Indian, Southeast Asian and Middle Eastern food, stroke researchers at Cedars-Sinai Medical Center think you may become a fan of one of their key spices.

The scientists created a new molecule from curcumin, a chemical component of the golden-colored spice turmeric, and found in laboratory experiments that it affects mechanisms that protect and help regenerate brain cells after stroke. Research scientist Paul A. Lapchak, Ph.D., director of Translational Research in the Department of Neurology at Cedars-Sinai Medical Center, will present these findings at the American Heart Association International Stroke Conference in Los Angeles on Wednesday, Feb. 9, at 6:15 p.m. PST.

Only one drug is now approved for ischemic stroke, which occurs when a clot blocks blood flow to the brain. Commonly called a "clot-busting drug," tissue plasminogen activator (tPA) is injected intravenously to dissolve clots and reinstate blood flow. If blood and oxygen are restored in time, consequences of the stroke, such as speech, memory, movement and other impairments, may be reduced.

The new curcumin-hybrid compound—CNB-001—does not attack clots but instead repairs stroke damage at the molecular level that feed and support the all-important brain cells, neurons.

Curcumin has been studied for its potential to treat brain injury and disease, and while the substance itself looks promising, it has several drawbacks, especially as an emergency stroke treatment, which must be quick to be effective: It is not well absorbed in the body, fails to reach its target in high concentrations, becomes depleted quickly, and is blocked from entering the brain by a natural protective mechanism called the blood-brain barrier.

"CNB-001 has many of the same benefits of curcumin but appears to be a better choice of compound for acute stroke because it crosses the blood-brain barrier, is quickly distributed in the brain, and moderates several critical mechanisms involved in neuronal survival," Lapchak says, adding that he and his colleagues expect the new drug to move to human clinical trials soon.

When brain tissue is deprived of blood and oxygen, a cascading series of interrelated events triggers at the molecular level, breaking down the normal electrical and chemical "signaling pathways" responsible for nourishing and supporting neurons. The environment quickly becomes toxic, killing brain cells and destroying their support structures.

Theoretically, interrupting these harmful events and restoring normal pathway function could prevent cell death and the memory and behavioral deficits that result, but it will take a cocktail of drugs or a drug capable of targeting many mechanisms to correct the many pathways damaged by stroke, Lapchak says.

CNB-001 protects brain cells from damage by repairing four major pathways. One mechanism also plays a major role in the growth and survival of neurons.

The drug reduced stroke-caused "motor deficits"—problems of muscle and movement control—in this laboratory study. It was effective when administered up to an hour after stroke, which correlates with about three hours in humans, the same time frame for which tPA is currently approved.

Lapchak and colleagues at the Salk Institute for Biological Studies used the same laboratory rabbit model to mimic human stroke that earlier researchers had employed before the clot-busting drug tPA entered clinical trials.

Patrick D. Lyden, M.D., chairman of Cedars-Sinai's Department of Neurology, helped lead a major trial that resulted in the Food and Drug Administration's 1996 approval of tPA, still considered the stroke treatment gold standard.

Those who cook Indian, Thai, Malay and Persian dishes know turmeric well for its zesty flavor, use in curries and for the rich color it imparts to food. Turmeric also has a long history of use in Ayurvedic and Chinese traditional medicine.

*Grants from the National Institute of Neurological Disorders and Stroke, part of the National Institutes of Health, supported the CNB-001 study (NS060685 to PAL).*

*Citation: American Heart Association International Stroke Conference Wednesday, Feb. 9 at 6:15 p.m*



## Simple marine worms distantly related to humans

**Two groups of lowly marine worms are related to complex species including vertebrates (such as humans) and starfish, according to new research.**

Previously thought to be an evolutionary link between simple animals such as jellyfish and the rest of animal life - the worms' surprising promotion implies that they have not always been as simple as they now appear.

Although the marine worms Xenoturbella and Acoelomorpha are very simple animals – they lack a developed nervous system or gut – they have been a source of much debate among zoologists. Acoelomorphs were reclassified in the 1990's as an early branch of evolution - the crucial link between the very simplest animals such as sponges and jellyfish and the rest of the animal kingdom including humans, starfish, insects and molluscs.



*Xenoturbella* innovations report

Now, in research published online today in Nature, an international team led by scientists from UCL (University College London) and the Université de Montréal have shown that neither type of worm is an early branch of evolution. They show that both groups descended from the same ancestor that gave rise to the complex groups of animals that includes vertebrates and starfish. This implies that the worms have in effect 'evolved backwards' into much simpler looking organisms.

Specimens of *Xenoturbella* were collected from the mud at the bottom of a Swedish fjord where it eats bivalve molluscs; the acoelomorphs are found in various marine environments - one called *Meara stichopi* even makes its home in the throat of a sea cucumber. Scientists compared hundreds of genes from both *Xenoturbella* and the Acoelomorpha with their counterparts from a whole range of animal species to determine their evolutionary relationships.

The results show that the two groups constitute a newly classified phylum (a major division of life), which the authors name the 'Xenacoelomorpha'. The xenacoelomorph phylum joins the three known phyla of deuterostomes: vertebrates (including humans), echinoderms (e.g. starfish) and hemichordates (acorn worms).



***An international research team led by Brown University has determined that the flatworm Acoelomorpha belongs as a sister clade to other bilateral animals. The finding means the worm is a product of the deepest split within the bilateral animals, the first evolutionary divergence within the group.*** Eric Rottinger/Kahikai.org

Professor Max Telford, from the UCL Department of Genetics, Evolution and Environment, and joint leader of the research said: "Because the simple Xenacoelomorpha are descended from the same ancestor that gave rise to complex groups such as vertebrates, echinoderms and hemichordates, these simple worms must have lost a lot of the complexity that they originally possessed."

Professor Telford said: "We can no longer consider the acoelomorphs as an intermediate between simple groups such as jelly fish and the rest of the animals. This means that we have no living representative of this stage of evolution: the missing link has gone missing!"

Professor Hervé Philippe from the Université de Montréal said: "This is the happy result of a more than ten year struggle with these highly unusual organisms that have proved very difficult to locate on the tree of life. Improvements in DNA sequencing technology and in mathematical methods to infer evolutionary history were key to solving the conundrum of *Xenoturbella* and the acoelomorphs"

[http://www.eurekalert.org/pub\\_releases/2011-02/uoca-tms020411.php](http://www.eurekalert.org/pub_releases/2011-02/uoca-tms020411.php)

## Treating mild strokes with clot-busting drug could save \$200 million annually, study shows

**CINCINNATI—Treating mild strokes with the clot-busting drug approved for severe stroke could reduce the number of patients left disabled and save \$200 million a year in disability costs, according to new research from the University of Cincinnati (UC).**

The study led by Pooja Khatri, MD, an associate professor in the department of neurology, examined the public health impact of treating mild strokes with the clot-busting drug intravenous tissue plasminogen activator (tPA). It is being presented Wednesday, Feb. 9, in Los Angeles at International Stroke Conference 2011, the annual meeting of the American Stroke Association.

The research is part of the Greater Cincinnati/Northern Kentucky Stroke Study, begun in 1993 at the UC College of Medicine, which is funded by the National Institutes of Health (NIH) and identifies all hospitalized and autopsied cases of stroke and transient ischemic attack (TIA) in a five-county region. The NIH also funded the study led by Khatri.

Researchers at UC analyzed hospital records from 437 patients at 16 sites in the Greater Cincinnati/Northern Kentucky Stroke Study region in 2005, the latest period for which complete records are available. The patients arrived at the hospital within 3.5 hours of experiencing symptoms, well within the 4.5-hour window for treatment with tPA. Of those 427 patients, 247 were diagnosed with mild ischemic stroke on a stroke severity scale.

Only four of the mild stroke patients (about 1.6 percent) received tPA, which is approved by the Food and Drug Administration for strokes caused by blood clots, known as ischemic strokes. It's the only acute stroke treatment proven to reduce disability, but remains untested for treating mild stroke because experts previously believed patients would recover with few lasting effects and tPA treatment carries a slight but significant risk of bleeding to the brain.

Of the remaining 243 mild stroke patients in the study, 150 (62 percent) were identified as likely candidates for the drug if the mildness of their stroke was disregarded as a reason to deny tPA treatment. Excluding patients with baseline disability (estimated at 37 percent), researchers assumed that 8 percent to 13 percent of the remaining patients would regain independence after their stroke if tPA was an effective treatment for this group.

Extrapolating to the U.S. population, the researchers said that if tPA proves effective for mild stroke, at least 2,000 fewer patients would be disabled from mild stroke each year. Assuming a moderate disability and conservatively estimating a lifetime cost of \$100,000 per patient, at least \$200 million in disability expenditures would be saved.

In the last five years, researchers conducting several studies have found that about one-third of patients who experienced mild strokes remained disabled three months after initial hospitalization.

"Currently, there is no standard of treatment for patients with the mildest strokes," says Khatri, a member of the UC Neuroscience Institute and division director of the acute stroke program at UC. "These findings raise the question of whether the mildest strokes should be treated with intravenous tPA."

For that answer, Khatri says, more study is needed with mild stroke patients included in future trials of the effectiveness [http://www.eurekalert.org/pub\\_releases/2011-02/w-hwy020911.php](http://www.eurekalert.org/pub_releases/2011-02/w-hwy020911.php) of clot-busting drugs.

### **Hearing with your nose: How nasal stem cells could tackle childhood hearing problems** ***Stem Cell scientists in Australia have found that patients suffering from hearing problems which began during infancy and childhood could benefit from a transplant of stem cells from their nose.***

The research, published today in STEM CELLS, reveals that mucosa-derived stem cells can help preserve hearing function during the early-onset of sensorineural hearing loss.

Sensorineural hearing loss is caused by the loss of sensory cells or neurons in the cochlea, the sensory organ of the inner ear responsible for hearing. The condition can have genetic causes, often arising during infancy and childhood, hindering cognitive development and leading to speech and language problems.

"One of the challenges in tackling this condition is that the regenerative ability of the human cochlea is severely limited", said lead author Dr. Sharon Oleskevich from the Hearing Research Group at The University of New South Wales. "It has been proposed that the transplantation of cells from other parts of the body could treat, prevent or even reverse hearing loss. The transplanted cells have the potential to repair tissue by replacing damaged cells and enhancing the survival of existing cells, preventing the condition from developing further."

To investigate the effects of this treatment, nasal stem cells were injected into the cochlea of mice displaying symptoms of hearing loss. Mice were chosen for this treatment as they display a similar decline in hearing function following infancy.

"The authors have used an interesting type of adult stem cell, related to mesenchymal stem cells, to reduce the extent of hearing loss. Since the cells did not integrate into the cochlea, it is likely that the effects from the adult stem cells were due to the release of factors to preserve function of the endogenous stem cells. Mesenchymal stem cells are known to provide factors to keep many types of cells healthy and functioning," said Jan Nolte, Associate Editor of STEM CELLS.

Patient hearing levels were examined using the auditory brainstem response assay, which determines the lowest sound level to which the brain responds, known as the hearing threshold.

The mice which received the transplanted cells were compared to mice who had not received the treatment a month later, revealing that the hearing threshold level in stem cell-transplanted mice was significantly lower.

"The results demonstrate a significant effect of nasal stem cell transplantations for sensorineural hearing loss," concluded Oleskevich. "These cells can be obtained easily from the nasal cavity making this transplantation a potential treatment for other human conditions including Parkinson's disease and cardiac infarction."

[http://seattletimes.nwsourc.com/html/nationworld/2014166303\\_toyota09.html](http://seattletimes.nwsourc.com/html/nationworld/2014166303_toyota09.html)

## **NASA engineers can't find electronic flaws in Toyotas**

By MATTHEW L. WALD The New York Times

**WASHINGTON — *There is no evidence that unintended accelerations in Toyota vehicles were caused by electronic flaws, the Transportation Department said Tuesday.***

The agency reached the conclusion after a 10-month investigation that said the mechanical causes were the same ones identified earlier by the National Highway Traffic Safety Administration (NHTSA): sticking accelerator pedals and floor-mat interference.

"The jury is back," said Ray LaHood, the transportation secretary. "The verdict is in. There is no electronic-based cause for unintended high-speed acceleration in Toyotas. Period."

An engineer from the National Aeronautics and Space Administration (NASA), brought in to help conduct the inquiry, was slightly less categorical but still emphatic. "It's very difficult to prove a negative," said Michael Kirsch, a principal engineer with NASA's Engineering and Safety Center.

But the electronic system for throttle controls in Toyotas would require two separate sensors to fail simultaneously in such a way that neither created an "error code" in the vehicle's onboard computer.

There were relatively few instances of even one sensor failing, said Kirsch, who added that investigators had access to Toyota's designs, engineering and warranty data.

In a statement, Steve St. Angelo, Toyota's chief quality officer for North America, said the automaker hoped the study would help put to rest questions about the reliability of Toyota's electronic systems.

The government said it was considering undertaking new research, on "the placement and design of accelerator and brake pedals, as well as driver usage of pedals, to determine whether design and placement can be improved to reduce pedal misapplication."

It is also considering proposing rules, by the end of this year, that would require a standard method to turn off the engine where the driver does not have to insert a key into the ignition. It is also considering a requirement for "event-data recorders," a step it has long resisted.

Many cars already have such recorders, simplified versions of an airplane's "black box," which capture data in the last few seconds before air bags are deployed and keep information like engine speed, brake and accelerator application and power of impact. And it is considering a broad research program on "the reliability and security of electronic-control systems," the department said in a statement.

The findings of the Toyota investigation were similar to those of a preliminary government report released in August. In fact, the finding vindicated not only Toyota but the safety agency itself.

"NHTSA, America's traffic-safety organization, was right all along," LaHood said.

He said the Transportation Department had ordered the search for an electronics problem because in the hearings on Capitol Hill, at which he testified last year, "just about every member of Congress didn't believe that we had found the problem, which was floor mats and the sticky pedals.

In claiming victory though, LaHood was far different in his tone toward Toyota than he was last year when news of the acceleration problems broke. At one point, during a congressional hearing, LaHood said that owners of recalled Toyotas should stop driving the vehicles and take them back to the dealers, though he quickly backtracked on the comments.

On Tuesday, he praised Toyota for its plans to establish a \$50 million safety center in Michigan.

LaHood and other officials were also quite diplomatic about a likely cause of the unintended accelerations — pushing on the accelerator instead of the brake. On Tuesday, department officials called these "pedal misapplications."

Toyota eventually recalled more than 11 million Toyota and Lexus vehicles worldwide because of floor mats and sticky accelerator pedals. The automaker also paid three fines totaling \$48.8 million, because, the Transportation Department said, Toyota had not reacted appropriately to reports of problems.

In a statement, the highway agency said Tuesday that NASA engineers evaluated the electronic circuitry in Toyota vehicles and analyzed more than 280,000 lines of software code for any potential flaws that could initiate unintended acceleration.

As with Tuesday's report, the preliminary examination given to Congress in August found no evidence of flawed electronics in vehicles that crashed. That examination found only one instance in which an accelerator pedal became trapped under a floor mat and none in which a pedal became stuck or sprang back too slowly.



The recalls have marred Toyota's reputation for high quality and safe vehicles, hurting sales for much of the year. In response to complaints, Toyota has begun to install a brake-override system, which allows the brake to stop the vehicle even if the accelerator is pressed simultaneously, as standard equipment across its lineup by the end of this year. The company also set up a panel so customer complaints are relayed more quickly to headquarters.

Toyota said its sales were down 0.4 percent in 2010; it was the only full-line automaker to report lower sales last year. Shares of Toyota rose 4 percent to close at \$88.57, gaining momentum as news of the report leaked out ahead of the announcement Tuesday afternoon.

<http://www.nytimes.com/2011/02/08/science/08tier.html>

## Social Scientist Sees Bias Within

By JOHN TIERNEY

**SAN ANTONIO — *Some of the world's pre-eminent experts on bias discovered an unexpected form of it at their annual meeting.***

Discrimination is always high on the agenda at the Society for Personality and Social Psychology's conference, where psychologists discuss their research on racial prejudice, homophobia, sexism, stereotype threat and unconscious bias against minorities. But the most talked-about speech at this year's meeting, which ended Jan. 30, involved a new "outgroup."

It was identified by Jonathan Haidt, a social psychologist at the University of Virginia who studies the intuitive foundations of morality and ideology. He polled his audience at the San Antonio Convention Center, starting by asking how many considered themselves politically liberal. A sea of hands appeared, and Dr. Haidt estimated that liberals made up 80 percent of the 1,000 psychologists in the ballroom. When he asked for centrists and libertarians, he spotted fewer than three dozen hands. And then, when he asked for conservatives, he counted a grand total of three.

"This is a statistically impossible lack of diversity," Dr. Haidt concluded, noting polls showing that 40 percent of Americans are conservative and 20 percent are liberal. In his speech and in an interview, Dr. Haidt argued that social psychologists are a "tribal-moral community" united by "sacred values" that hinder research and damage their credibility — and blind them to the hostile climate they've created for non-liberals.

"Anywhere in the world that social psychologists see women or minorities underrepresented by a factor of two or three, our minds jump to discrimination as the explanation," said Dr. Haidt, who called himself a longtime liberal turned centrist. "But when we find out that conservatives are underrepresented among us by a factor of more than 100, suddenly everyone finds it quite easy to generate alternate explanations."

Dr. Haidt (pronounced height) told the audience that he had been corresponding with a couple of non-liberal graduate students in social psychology whose experiences reminded him of closeted gay students in the 1980s. He quoted — anonymously — from their e-mails describing how they hid their feelings when colleagues made political small talk and jokes predicated on the assumption that everyone was a liberal.

"I consider myself very middle-of-the-road politically: a social liberal but fiscal conservative. Nonetheless, I avoid the topic of politics around work," one student wrote. "Given what I've read of the literature, I am certain any research I conducted in political psychology would provide contrary findings and, therefore, go unpublished. Although I think I could make a substantial contribution to the knowledge base, and would be excited to do so, I will not."

The politics of the professoriate has been studied by the economists Christopher Cardiff and Daniel Klein and the sociologists Neil Gross and Solon Simmons. They've independently found that Democrats typically outnumber Republicans at elite universities by at least six to one among the general faculty, and by higher ratios in the humanities and social sciences. In a 2007 study of both elite and non-elite universities, Dr. Gross and Dr. Simmons reported that nearly 80 percent of psychology professors are Democrats, outnumbering Republicans by nearly 12 to 1.

The fields of psychology, sociology and anthropology have long attracted liberals, but they became more exclusive after the 1960s, according to Dr. Haidt. "The fight for civil rights and against racism became the sacred cause unifying the left throughout American society, and within the academy," he said, arguing that this shared morality both "binds and blinds."

"If a group circles around sacred values, they will evolve into a tribal-moral community," he said. "They'll embrace science whenever it supports their sacred values, but they'll ditch it or distort it as soon as it threatens a sacred value." It's easy for social scientists to observe this process in other communities, like the fundamentalist Christians who embrace "intelligent design" while rejecting Darwinism. But academics can be selective, too, as Daniel Patrick Moynihan found in 1965 when he warned about the rise of unmarried parenthood and welfare dependency among blacks — violating the taboo against criticizing victims of racism.



“Moynihan was shunned by many of his colleagues at Harvard as racist,” Dr. Haidt said. “Open-minded inquiry into the problems of the black family was shut down for decades, precisely the decades in which it was most urgently needed. Only in the last few years have liberal sociologists begun to acknowledge that Moynihan was right all along.”

Similarly, Larry Summers, then president of Harvard, was ostracized in 2005 for wondering publicly whether the preponderance of male professors in some top math and science departments might be due partly to the larger variance in I.Q. scores among men (meaning there are more men at the very high and very low ends). “This was not a permissible hypothesis,” Dr. Haidt said. “It blamed the victims rather than the powerful. The outrage ultimately led to his resignation. We psychologists should have been outraged by the outrage. We should have defended his right to think freely.”

Instead, the taboo against discussing sex differences was reinforced, so universities and the National Science Foundation went on spending tens of millions of dollars on research and programs based on the assumption that female scientists faced discrimination and various forms of unconscious bias. But that assumption has been repeatedly contradicted, most recently in a study published Monday in *The Proceedings of the National Academy of Sciences* by two Cornell psychologists, Stephen J. Ceci and Wendy M. Williams. After reviewing two decades of research, they report that a woman in academic science typically fares as well as, if not better than, a comparable man when it comes to being interviewed, hired, promoted, financed and published.

“Thus,” they conclude, “the ongoing focus on sex discrimination in reviewing, interviewing and hiring represents costly, misplaced effort. Society is engaged in the present in solving problems of the past.” Instead of presuming discrimination in science or expecting the sexes to show equal interest in every discipline, the Cornell researchers say, universities should make it easier for women in any field to combine scholarship with family responsibilities.

Can social scientists open up to outsiders’ ideas? Dr. Haidt was optimistic enough to title his speech “The Bright Future of Post-Partisan Social Psychology,” urging his colleagues to focus on shared science rather than shared moral values. To overcome taboos, he advised them to subscribe to *National Review* and to read Thomas Sowell’s “A Conflict of Visions.”

For a tribal-moral community, the social psychologists in Dr. Haidt’s audience seemed refreshingly receptive to his argument. Some said he overstated how liberal the field is, but many agreed it should welcome more ideological diversity. A few even endorsed his call for a new affirmative-action goal: a membership that’s 10 percent conservative by 2020. The society’s executive committee didn’t endorse Dr. Haidt’s numerical goal, but it did vote to put a statement on the group’s home page welcoming psychologists with “diverse perspectives.” It also made a change on the “Diversity Initiatives” page — a two-letter correction of what it called a grammatical glitch, although others might see it as more of a Freudian slip.

In the old version, the society announced that special funds to pay for travel to the annual meeting were available to students belonging to “underrepresented groups (i.e., ethnic or racial minorities, first-generation college students, individuals with a physical disability, and/or lesbian, gay, bisexual, or transgendered students).” As Dr. Haidt noted in his speech, the “i.e.” implied that this was the exclusive, sacred list of “underrepresented groups.” The society took his suggestion to substitute “e.g.” — a change that leaves it open to other groups, too. Maybe, someday, even to conservatives.

***This article has been revised to reflect the following correction: Correction: February 10, 2011***

*Because of an editing error, the Findings column on Tuesday, about political bias among social scientists, omitted the last four words of a sentence that countered the notion that female scientists face discrimination and various forms of unconscious bias. The sentence should have read: But that assumption has been repeatedly contradicted, most recently in a study published Monday in The Proceedings of the National Academy of Sciences by two Cornell psychologists, Stephen J. Ceci and Wendy M. Williams.*

<http://www.bbc.co.uk/news/health-12404473>

## **Study highlights medical split on breast cancer surgery**

**By Anna Browning Reporter**

### ***Removing cancerous lymph nodes from some women with breast cancer has no benefit, US scientists have revealed in a new study.***

But while the findings may have been hailed in parts of the media as a revolutionary approach to combating breast cancer, it has also revealed divisions among cancer specialists in the UK on how best to treat the disease.

While some hope the study will bring widespread change to practice - some UK units already operate a less surgically-aggressive approach - others urge caution about the findings.

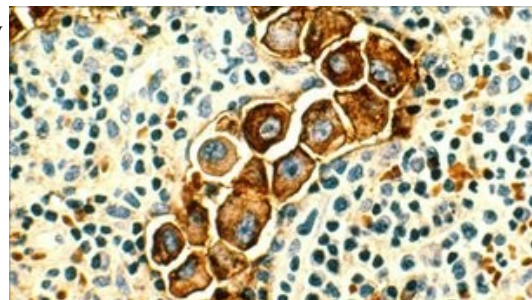
The study, published in the *Journal of the American Medical Association*, found that in women with early stage cancer the standard practice of removing cancerous nodes made no difference to survival rates.

They also found that carrying out the painful procedure - which can leave women with lasting arm swelling, stiffness and pain - made no difference to whether cancer returned.

The study, which involved about 850 women, follows a trend away from radical surgery in combating breast cancer in recent years.

Rates of mastectomy (the removal of the breast) are declining, but the removal of nodes as a way of preventing the spread of cancer, has remained standard procedure, particularly in the US.

All those taking part in the clinical trial, between 1999 and 2004, had had initial biopsies showing cancer had spread to one or two nearby lymph nodes.



***Lymph node showing cancer cells Removing lymph nodes is a painful procedure which can leave lasting problems***

They were then assigned at random to have 10 more more additional nodes removed or none at all.

They were also treated with lumpectomies to remove their tumours and a common type of radiation that covers the breast and underarm area. Most also had chemotherapy, hormone treatment, or both.

The researchers were led by Armando Giuliano of Saint John's Health Center, in Santa Monica, California.

### **'Practice-changing'**

Professor Ian Ellis, professor of cancer pathology at the University of Nottingham, said the study was "very powerful" and had been conducted in an "exemplary way".

"You can't knock it, it should be practice changing," he said, but acknowledged units in the UK were very "polarised". "It sometimes takes more than one study to change people's minds. In the UK doctors are a little bit conservative, they want more evidence."

He said a trial of 3,000 women conducted in Edinburgh about 15 years ago, and which produced similar results, had failed to change practice across the UK, but that this study vindicated his unit and others'.

"This shows centres doing less aggressive therapy were correct in their approach."

Dr Rachel Greig, senior policy officer at Breakthrough Breast Cancer charity said the findings were "exciting", particularly as they corroborated past findings, but was cautious on how quickly practices would change.

"They could change the way some women are treated for breast cancer in the future," she said.

"This is important as it may mean these women can avoid unnecessary lymph node surgery. The findings agree with past research so we eagerly await further developments in this area."

Professor Michael Baum, retired breast surgeon and director of the clinical trials group at University College London, said he was amused at the research.

"What they are doing is reinventing the wheel," he told the BBC. "I have been preaching this for decades."

"We have known for 20 years or more that leaving an untreated lymph node behind that contains a tumour does not impair long-term survival."

However, he said, the study would be influential in changing practice and patients would benefit.

But Professor Robert Mansel, professor of surgery at University of Wales College of Medicine, Cardiff, and expert in breast cancer research, said it was a very controversial area with a lot of practice "based on feelings, not data".

### **Caution urged**

He currently favours the removal of lymph nodes, believing the research on leaving them intact to be inconclusive so far.

He urged caution about the US study, pointing to "lots of warning signs" in the paper, such a failure to recruit as many women to the study as they would have liked - meaning the trial was "under powered".

When faced with the prospect of lymph nodes not being removed, a lot of patients failed to enter the trial, he said. He also pointed to the study's five-year follow-up, which he said was quite short. "Breast cancer, if nothing else, is a long-term disease, which makes this study only half way to being reliable".

On the differences of opinion in the field, he said: "We are using the same evidence, but interpreting it differently." "It's a classic problem in cancer management; we don't have the answer."

He said a European trial, Amaros, which he is heading and is due to publish its results like year, would be more likely to change practice.

Like the US trial, this trial takes an initial biopsy, but it then gives radiotherapy to the remaining nodes to see if this is in fact enough and there was no more need for surgery.

"We are on the cusp of finding out the information, but there isn't enough of it. If you make changes before you have the data that you can get a shock. Nobody is right or wrong, it's a philosophy.

"When Amos reports hopefully we should get a definitive answer. "We may well change practice, but it's going to take two or three years before we can say definitively one way or another."

<http://www.physorg.com/news/2011-02-nanonets-rust-boost-agent-hydrogen.html>

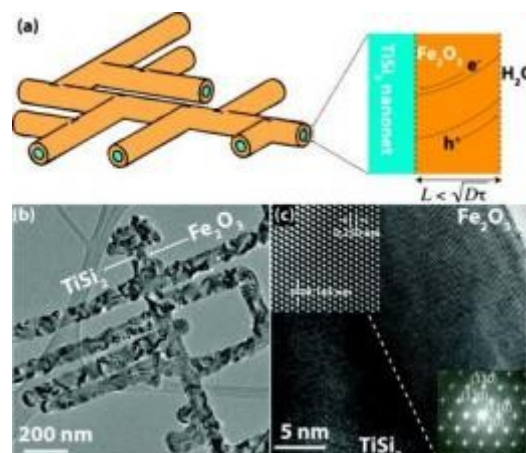
## Nanonets give rust a boost as agent in water splitting's hydrogen harvest

**Coating a lattice of tiny wires called Nanonets with iron oxide – known more commonly as rust – creates an economical and efficient platform for the process of water splitting, an emerging clean fuel science that harvests hydrogen from water, Boston College researchers report in the online edition of the *Journal of the American Chemical Society*.**

Assistant Professor of Chemistry Dunwei Wang and his clean energy lab pioneered the development of Nanonets in 2008 and have since shown them to be a viable new platform for a number of energy applications by virtue of the increased surface area and improved conductivity of the nano-scale netting made from titanium disilicide, a readily available semiconductor.

Wang and his team report that coating the Nanonets with hematite, the plentiful mineral form of iron oxide, showed the mineral could absorb light efficiently and without the added expense of enhancing the material with an oxygen evolving catalyst.

The results flow directly from the introduction of the Nanonet platform, Wang said. While constructed of wires 1/400th the size of a human hair, Nanonets are highly conductive and offer significant surface area. They serve dual roles as a structural support and an efficient charge collector, allowing for maximum photon-to-charge conversion, Wang said.



*Boston College researchers have tested their Nanonet design as a platform for clean energy applications. Most recently, coating the highly conductive titanium disilicide core (a) with hematite, the mineral form of iron oxide, or rust, dramatically improved the performance of the material at its fundamental state. Transmission electron microscopy image (b) shows the structural complexity of the Nanonet and additional images (c) detail the hematite Nanonet spacing, as well as the electron diffraction pattern of hematite (lower right corner). Credit: Journal of the American Chemical Society*

"Recent research has shown that the use of a catalyst can boost the performance of hematite," said Wang. "What we have shown is the potential performance of hematite at its fundamental level, without a catalyst. By using this unique Nanonet structure, we have shed new light on the fundamental performance capabilities of hematite in water splitting."

On its own, hematite faces natural limits in its ability to transport a charge. A photon can be absorbed, but has no place to go. By giving it structure and added conductivity, the charge transport abilities of hematite increase, said Wang. Water splitting, a chemical reaction that separates water into oxygen and hydrogen gas, can be initiated by passing an electric current through water. But that process is expensive, so gains in efficiency and conductivity are required to make large-scale water splitting an economically viable source for clean energy, Wang said.

"The result highlights the importance of charge transport in semiconductor-based water splitting, particularly for materials whose performance is limited by poor charge diffusion," the researchers report in the journal. "Our design introduces material components to provide a dedicated charge transport pathway, alleviates the reliance on the materials' intrinsic properties, and therefore has the potential to greatly broaden where and how various existing materials can be used in energy-related applications."

More information: <http://pubs.acs.org> ... 21/ja110741z

<http://www.physorg.com/news/2011-02-sector-responsible-drug-discoveries.html>

## Researchers find public sector research responsible for many new drug discoveries

**Researchers from Boston University School's of Medicine (BUSM), Management (SMG) and Law (LAW), along with collaborators from the National Institutes of Health, believe that public-sector research has had a more immediate effect on improving public health than was previously realized. The findings, which appear as a Special Article in the February 10th issue of *The New England Journal of Medicine*, have economic and policy implications.**

Historically, public sector research institutions (PSRI) have not participated in any major way in the downstream, applied phase of drug discovery, in which the actual products are discovered and patented. However, in the mid-1970s, the newly emerging tools of biotechnology allowed PSRIs to create and patent biologic drug candidates and discover and patent small molecule drugs. At that time, all products created in academic institutions were owned by the government, which granted only nonexclusive licenses.

In 1980, Congress passed two pieces of legislation that transformed the ownership, management and transfer of intellectual property that is created by PSRIs. First, the Bayh–Dole Act allowed universities, nonprofit



research institutes and teaching hospitals to own the intellectual property resulting from federally funded research and to license it according to terms of their choosing. Second, the Stevenson–Wydler Technology Innovation Act as amended by the Federal Technology Transfer Act of 1986, provided a corresponding authority to federal laboratories. Under this new approach, inventions that arose from PSRIs, in addition to being freely published in the scientific literature, could also be converted into intellectual property and transferred through license agreements to the private sector for commercialization and public use.

In order to quantitate the contribution of public-sector research to the applied-research phase of drug discovery, the researchers identified new drugs and vaccines approved by the Food and Drug Administration (FDA) and classified them according to their therapeutic category and potential therapeutic effect. The researchers found that during the past 30 years, 153 new FDA-approved drugs, vaccines, or new indications for existing drugs were discovered through research carried out in PSRIs. These drugs included 93 small-molecule drugs, 36 biologic agents, 15 vaccines, eight in-vivo diagnostic materials, and one over-the-counter drug. Current and former Boston University researchers were responsible for four of those 153 new drugs, one of which was developed based on research conducted at the University and Boston Medical Center.

"We believe that our study supports the concept that the emergence of biotechnology in the mid-1970s, combined with policy changes implemented in the early 1980s regarding the ownership and management of the intellectual property of PSRIs, allowed these institutions to play an important role in the downstream, applied phase of drug discovery," said lead author Ashley J. Stevens, D.Phil (Oxon), CLP, a lecturer at BUSM as well as Special Assistant to the Vice President for Research, Technology Development and a Senior Research Associate, ITEC, SMG. He is also currently the President of the Association of University Technology Managers.

According to the researchers, the data also suggest that PSRIs tend to discover drugs that have a disproportionately important clinical effect. "Slightly over half of these drugs were for the treatment or prevention of cancer or infectious diseases. Furthermore, drugs discovered by PSRIs received Priority Review by the FDA at twice the rate as for all FDA drug approvals, indicating that PSRI discovered drugs were expected to have a disproportionately high therapeutic impact," added Stevens.

"We hope our research will help inform the amplified conversation taking place around innovation policy in the US and abroad," said co-author Jonathan Jensen, MBA, Director, Business Development, Technology Development at Boston University. "The factors involved in bringing a single one of these drugs to market are complex. With a more comprehensive understanding of the contribution of the public sector to the development of FDA approved drugs, as our work attempts to establish, one can better appreciate and further study the factors involved in the transfer of knowledge from the public to the private sector," he added.

*Provided by Boston University Medical Center*

[http://www.eurekalert.org/pub\\_releases/2011-02/sfmm-sfm020111.php](http://www.eurekalert.org/pub_releases/2011-02/sfmm-sfm020111.php)

### **Study finds magnesium sulfate may offer protection from cerebral palsy**

**SAN FRANCISCO – In a study to be presented today at the Society for Maternal-Fetal Medicine's (SMFM) annual meeting, The Pregnancy Meeting™, in San Francisco, researchers will present findings that showed that in rats, the use of magnesium sulfate (Mg) significantly reduced the neonatal brain injury associated with maternal inflammation or maternal infection.**

Magnesium sulfate is sometimes used during preterm labor to reduce the risk of neonatal brain injury. In 2010 the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine issued an opinion that "available evidence suggests that magnesium sulfate given before anticipated preterm birth reduces the risk of cerebral palsy in surviving infants."

"We knew there were indications from other studies that magnesium sulfate might protect a preterm fetus from cerebral palsy, but we wanted to demonstrate direct and conclusive protective effect on the offspring brain in cases of maternal inflammation" said Ron Beloosesky, M.D., one of the study's authors. "We wanted to learn more about the protective effects of Mg in cases where maternal inflammation causes preterm birth, so we used the very sensitive diffusion tensor imaging, Magnetic Resonance Imaging to study how Mg works."

Beloosesky and his colleagues studied pregnant Sprague-Dawley rats at 18 days gestation that received i.p. LPS (500 µg/kg) or saline at time 0. Dams were randomized to treatment with s.c. saline or Mg (270 mg/kg loading followed by 27 mg/kg q20 min) for two hours prior to and following the i.p. LPS or saline. Pups were delivered spontaneously (e21) and allowed to mature until postnatal day 25. Female offspring (4-8 per group) were examined under isoflurane anesthesia by MRI brain imaging and analyzed using voxel based analysis (VBA) after spatial normalization. T2 relaxation time was used to assess for white matter injury and diffusion tensor imaging for Fractional Anisotropy (FA) comparison.



The results showed that offspring of LPS-treated dams exhibited significantly increased T2 levels, and reduced FA levels in white and gray matter (eg, corpus callosum, thalamus, hippocampus), consistent with diffuse cerebral injury. In contrast, offspring of Mg-treated LPS dams demonstrated similar T2 and FA levels as control in both white and gray matter.

The study concluded that Mg treatment significantly reduced evidence of neonatal brain injury associated with maternal LPS. These studies suggest that maternal Mg therapy may be most effective in human preterm deliveries associated with maternal/fetal inflammation.

"The next step, said Beloosesky, "is to do more studies to understand exactly how the Mg works and protects the fetal brain."

[http://www.eurekalert.org/pub\\_releases/2011-02/foas-sga021011.php](http://www.eurekalert.org/pub_releases/2011-02/foas-sga021011.php)

### **Salivary glands as organs of immunity: New research makes oral immunization easier to swallow**

#### ***New research in the FASEB Journal suggests that vaccinating through salivary glands may provide protection against a wide range of diseases***

If you don't like shots or needles, you're in luck. New research published online in The FASEB Journal (<http://www.fasebj.org>) gives the development of new oral vaccinations a shot in the arm thanks to discoveries involving the salivary glands of mice. In addition, this research report also offers a tantalizing glimpse of vaccines that could prevent infection at mucosal surfaces, even if direct injections into the body fail to cause immunity. This technique may be effective for a wide range of diseases from influenza to cholera.

"Our work highlights the ability of the salivary glands to act as an alternative mucosal route for administering vaccines, which would lead to protective immune responses both locally and systemically," said Lucille London, Ph.D., a researcher involved in the work from the School of Dental Medicine and Department of Oral Biology and Pathology at Stony Brook University in Stony Brook, NY. "Thus, in the future, salivary gland inoculation may become a clinically acceptable method in which to vaccinate groups of individuals against new and emerging pathogenic challenges."

To make this advance, the researchers studied two groups of mice. The first group received live cytomegalovirus directly into their salivary glands. These mice demonstrated an immune response in the salivary glands, and the researchers observed an increase in the number and types of cells associated with antibodies that were protective in the saliva. Importantly, these antibodies were also found in other mucosal secretions and in the serum of these mice, suggesting that these proteins spread to other locations in the body. Additionally, the researchers observed structural and functional changes in the immunized salivary glands, causing them to resemble lymph node-like structures commonly seen in injection-based immunizations. The second group of mice was given an inactive virus that did not cause an infection in the salivary glands. These mice demonstrated no active immune response when compared to the first group. When both sets of mice were exposed to the same virus at a later time, only the group immunized with an active virus was protected from future infection. This discovery opens the doors for similar research involving the use of weakened viruses to determine if they will also confer immunity through salivary glands.

"It's no fun for doctors or parents when kids struggle during routine immunization," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "It's even less fun when you are dealing with adults who are deathly afraid of shots in various parts of their body. This work shows that salivary glands may become the first line of defense in active and passive immunization."

[http://www.eurekalert.org/pub\\_releases/2011-02/uom-mar020611.php](http://www.eurekalert.org/pub_releases/2011-02/uom-mar020611.php)

### **MU, ASU researchers' discovery could change views of human evolution**

#### ***3.2 million-year-old human predecessor had arches in feet***

COLUMBIA, Mo. – Feet arches give humans a spring in their steps, shock absorbing abilities, and stiff platforms to propel themselves forward, allowing them to walk upright consistently. Now, researchers at the University of Missouri and Arizona State University have found proof that arches existed in a predecessor to the human species that lived more than 3 million years ago. This discovery could change scientists' views of human evolution. The study is being published this week in Science.



*University of Missouri and Arizona State University researchers have found a bone that indicates human ancestors had arches in their feet, a major evolutionary shift for "Lucy" and her species. Elizabeth Harmon*

Carol Ward, an MU researcher in the Department of Pathology and Anatomical Sciences at the MU School of Medicine, and William Kimbel and Donald Johanson, director and founding director of the Institute of Human Origins at Arizona State University, studied a 3.2 million-year-old fourth metatarsal of *Australopithecus afarensis*. A team from the Institute of Human Origins and National Museum of Ethiopia led by Kimbel discovered the fossil in Hadar, Ethiopia. The species is often referred to as "Lucy," the nickname of the most complete fossil skeleton of the species to be discovered.

The foot bone suggests that these hominids had stiff, arched feet, similar to humans. *Australopithecus afarensis* had smaller brains and stronger jaws than humans, and scientists have known the animals walked upright on two feet. However, researchers have not known whether Lucy and her kin were more versatile creatures than humans and spent time climbing through the trees.

"Now that we know Lucy and her relatives had arches in their feet, this affects much of what we know about them, from where they lived to what they ate and how they avoided predators," said Ward, professor of integrative anatomy. "The development of arched feet was a fundamental shift toward the human condition, because it meant giving up the ability to use the big toe for grasping branches, signaling that our ancestors had finally abandoned life in the trees in favor of life on the ground."

With human-like arches in its feet, *Australopithecus afarensis* was able to roam the countryside and leave the forest to forage for food when necessary. With its strong jaws, *Australopithecus* also could eat several types of food, including fruit, seeds, nuts and roots. Combining their strong jaws and their new skill of walking, Lucy and her relatives were able to live in open areas as well as wooded ones.

*Australopithecus* was a new kind of hominin, fundamentally different from earlier species like *Ardipithecus ramidus*, which preceded Lucy and was not committed to walking upright on the ground. Instead, *Ardipithecus ramidus* moved on all four feet or upright depending on the situation, and had powerful grasping feet.

"Arches in the feet are a key component of human-like walking because they absorb shock and also provide a stiff platform so that we can push off from our feet and move forward," Ward said. "People today with 'flat feet' who lack arches have a host of joint problems throughout their skeletons. Understanding that the arch appeared very early in our evolution shows that the unique structure of our feet is fundamental to human locomotion. If we can understand what we were designed to do and the natural selection that shaped the human skeleton, we can gain insight into how our skeletons work today. Arches in our feet were just as important for our ancestors as they are for us."

"This fourth metatarsal is the only one known of *A. afarensis* and is a key piece of evidence for the early evolution of the uniquely human way of walking," Kimbel said. "The ongoing work at Hadar is producing rare parts of the skeleton that are absolutely critical for understanding how our species evolved."

[http://www.eurekalert.org/pub\\_releases/2011-02/aha-msp020311.php](http://www.eurekalert.org/pub_releases/2011-02/aha-msp020311.php)

### **Most stroke patients not getting clot-busting treatment in timely manner**

***Less than one-third of acute stroke patients treated with intravenous tissue plasminogen activator (tPA) receive the clot-busting drug within 60 minutes of their hospital arrival, according to research presented at the American Stroke Association's International Stroke Conference 2011.***

The research is simultaneously published in *Circulation: Journal of the American Heart Association*.

The drug is a proven intervention for acute ischemic stroke patients, but can only be given within 4.5 hours after stroke onset and has the greatest benefits when given earlier in that timeframe.

Despite proven benefits, guidelines recommendations and explicit goals for administering tPA in a timely manner, the drug's administration has not been well studied, said Gregg C. Fonarow, M.D., lead author of the study and professor of cardiovascular medicine at the University of California-Los Angeles.

In abstract 205, Fonarow and colleagues reported the frequency, patient and hospital characteristics, trends and outcomes of ischemic stroke with door-to-needle times of 60 minutes or less.

They analyzed data from 1,082 hospitals from the American Heart Association/American Stroke Association's Get With The Guidelines®–Stroke quality improvement program between April 2003 and September 2009. Specifically, the researchers looked at 25,504 acute ischemic stroke patients treated with tPA within three hours of symptom onset.

They found during that time, 6,790, or 26.6 percent, received tPA in 60 minutes or less – with only modest improvement over the past 6.5 years – from 19 percent in 2003 to 29 percent in 2009.

Patients who were younger, male, white and had no prior stroke were most likely to receive the therapy within the 60-minute window, Fonarow said.

"It is a concern that older patients, women and black patients were less likely to receive timely tPA administration," he said. "It's also notable that the symptom onset-to-arrival times were shorter in patients with

door-to-needle times of greater than 60 minutes, suggesting that hospitals were taking a more relaxed approach to the administration of tPA in earlier arriving patients."

Hospitals that had greater annual volumes of tPA-treated stroke patients were more likely to administer the therapy within 60 minutes of hospital arrival.

"This suggests that greater hospital team experience translates into improved performance," said Fonarow, immediate-past chair of the Get With The Guidelines Steering Committee.

The proportion of patients with door-to-needle times of 60 minutes or less varied widely by hospital. Some hospitals did not achieve tPA administration within the ideal time frame for any patient. Other hospitals achieved door-to-needle times of 60 minutes or less in 80 percent or more of patients.

In abstract 146, the team also demonstrated that in-hospital mortality was significantly lower among patients treated more timely with tPA, and there were fewer complications with more timely treatment.

"These findings demonstrate for the first time that shorter door-to-needle times improve the likelihood that acute ischemic stroke patients will survive," Fonarow said.

The study identifies substantial opportunities nationally for improving the speed of tPA therapy initiation in acute ischemic stroke patients, he said.

"These findings suggest there is a critical need for a targeted campaign tailored to increase the portion of patients with door-to-needle times 60 minutes or less, such as the recently launched American Stroke Association Target®: Stroke initiative," Fonarow said. "Nearly 1,000 hospitals across the country are now registered to use Target: Stroke information and tools to improve their door-to-needle time for administering tPA to appropriate stroke patients."

*Co-authors are Eric E. Smith, M.D., M.P.H.; Jeffrey L. Saver, M.D.; Mathew J. Reeves, Ph.D.; Deepak L. Bhatt, M.D., M.P.H.; Maria V. Grau-Sepulveda, M.D., M.P.H.; DaiWai M. Olson, Ph.D., R.N.; Adrian F. Hernandez, M.D., M.H.S.; Eric D. Peterson, M.D., M.P.H.; and Lee H. Schwamm, M.D. Author disclosures are on the manuscript.*

[http://www.eurekalert.org/pub\\_releases/2011-02/aha-fds020311.php](http://www.eurekalert.org/pub_releases/2011-02/aha-fds020311.php)

### **Final data show experimental agent better than aspirin at preventing stroke**

***A new anti-clotting agent is vastly superior to aspirin at reducing stroke risk (1.6 percent per year versus 3.6 percent per year) in atrial fibrillation (AF) patients unable to take stronger drugs, according to final data reported today at the American Stroke Association's International Stroke Conference 2011.***

Researchers found the drug also works better in people with a history of stroke or a warning stroke.

Atrial fibrillation is a heartbeat abnormality that can cause blood clots which raise the risk of stroke, particularly in the elderly.

The AVERROES: Apixaban Versus Acetylsalicylic Acid (ASA) to Prevent Strokes trial is a randomized trial of 5,600 AF patients at moderate to high risk of stroke who were not willing or able to take oral vitamin-K antagonists like warfarin, a drug commonly prescribed to prevent blood clots in people with AF. They were treated at 520 medical centers worldwide. A May 2010 interim analysis found evidence that the investigational oral drug apixaban was so much more superior to aspirin that the researchers were advised to end the trial early, said Hans-Christoph Diener, M.D., professor and chairman, Department of Neurology and Stroke Center, University Hospital Essen, Essen, Germany.

In releasing the study's final results, he reported that apixaban was far superior to aspirin at preventing stroke or systemic embolism (blood clot) and was also very safe. The drug blocks factor Xa, a crucial step in blood clot formation, said Diener, co-chair of the study's adjudication committee.

"Apixaban was highly superior to aspirin. We had not anticipated that apixaban would show such a big difference compared with aspirin while showing no significant increase in major bleeds," he said. "Everyone had expected that a more powerful drug like apixaban would be associated with more severe bleeding complications compared to aspirin, but it wasn't."

The study's primary endpoint was the reduction of ischemic stroke (stroke caused by blockages in the brain's circulation), hemorrhagic stroke (stroke due to bleeding in the brain) and systemic embolism (blockages due to blood clots elsewhere in the body), he said. The primary safety endpoint was major bleeding incidents.

Up to 50 percent of all AF patients with moderate or high stroke risk are unsuitable for the most effective class of anti-clotting treatment known as vitamin K antagonists (VKA). That class includes the well-known drug warfarin.

All of the AVERROES patients were unsuitable for VKA therapy, which carries an increased risk of hemorrhage and requires frequent blood testing to monitor its effectiveness. For such patients the only alternate treatment is aspirin, which is just modestly effective, Diener said.



The patients in this study, all over age 50, were at moderate to high risk because they had at least one stroke risk factor in addition to AF, such as being age 75 or older, having high blood pressure, heart failure, diabetes or having a history of stroke or transient ischemic attack (a possible precursor of stroke), he explained.

Patients were randomized to receive either apixaban at 5 milligrams (mg) twice a day (2.5 mg twice a day in selected patients) or between 81 mg and 324 mg of aspirin per day. The study's double-dummy design mandated that patients randomized to receive apixaban took an aspirin-placebo and those randomized to receive aspirin got an apixaban-placebo, he explained.

During an average of 1.1 years of follow up, the researchers found 51 strokes or systemic embolism events in the 2,808 patients taking apixaban compared to 113 strokes and systemic embolic events in the 2,791 patients taking aspirin. That represents an annual rate of 1.6 percent for apixaban vs. 3.6 percent for aspirin, meaning apixaban carries about half the relative risk of stroke or systemic embolism compared to aspirin. Although bleeding events were slightly higher with apixaban, the difference fell short of statistical significance.

The researchers will also report on a subgroup of patients with a history of stroke or transient ischemic attack (TIA), often a precursor to stroke.

"If validated by future studies I think this is the end of aspirin as a drug to prevent stroke in patients with AF," he added.

Diener said the study's major limitation is the limited time period of observation, shortened further by the study's early conclusion. "AF patients need anticoagulation for the rest of their lives and we would have liked to see a much longer duration of the trial," he said.

"By evaluating the use of apixaban as a replacement for aspirin in AF patients who are unsuitable for VKA therapy, the AVERROES study is addressing an important unmet clinical need."

*Co-authors are Salim Yusuf M.D., Ph.D.; John Eikelboom, M.D.; Martin O. O'Donnell, M.D.; and Stuart J. Connolly, M.D. Disclosures are on the abstract. Bristol-Myers Squibb and Pfizer funded the study.*

<http://www.newscientist.com/article/mg20927993.800-spaghetti-junction-bridges-gaps-in-broken-spines.html>

## Spaghetti junction bridges gaps in broken spines

\* 10 February 2011 by Andy Coghlan

***INSPIRED by hollow spaghetti called bucatini, researchers in Italy have developed implants that help spinal cords regrow.***

Rats with spinal cord injuries recovered mobility in their hind legs, raising hope that the approach might one day help people with paraplegia.

The "bucacini project" is one of several around the world pioneering biodegradable scaffolds to bridge spinal cord injuries. Along with scar tissue, one of the main barriers to healing is the development of fluid-filled cysts at the site of the injury over the ensuing months. The idea of the implants is to create tiny conduits to guide formation of new nerve fibres, or axons, across this fluid-filled space.

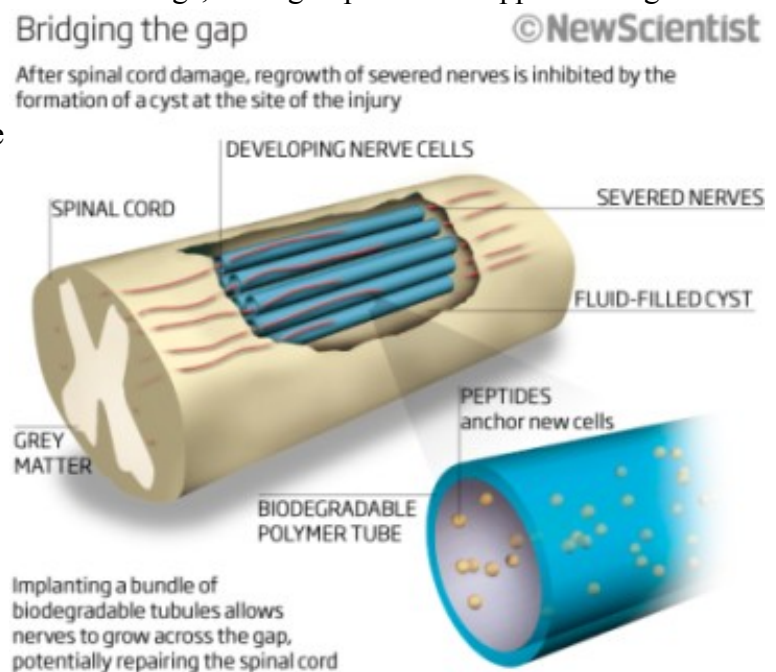
"These tubes provide the reference points for the cells, and tissue starts to build up," says Angelo Vescovi of the University of Milan-Bicocca.

Vescovi and colleague Fabrizio Gelain built hollow "nano-conduits" 2 to 3 millimetres long and about 0.5 millimetres across, from two biodegradable plastics: polycaprolactone and PLGA. To make surfaces more "sticky", they coated them with chemical hooks called self-assembling peptides, which help to anchor cells along the inside and outside of the tube.

***Pasta-inspired implants have helped rats with spinal cord injuries move their hind legs again – the approach might one day help people with paraplegia***

Finally, the researchers filled the tubules with a gel containing natural growth factors that stimulate nerve repair and growth. They then implanted bundles of the tubules into cysts that had formed where the spinal cords of rats had been damaged.

Six months later, Vescovi and Gelain found that new nerve fibres had grown all the way through many of the microscopic channels. Some had also grown between the tubes, together with all the other types of supporting





cells that nerves need for survival. New blood vessels had also grown, providing a blood supply (ACS Nano, DOI: 10.1021/nn102461w). "Where once there was just a cyst, you have pseudo-tissue that looks just like normal spinal cord tissue," says Vescovi. Treated animals recovered some mobility in their hind legs, which remained paralysed in the untreated control animals. Vescovi also found chemical markers in the spinal tissue that suggested repair was still under way.

"One of the most striking results is the extent and alignment of axonal growth," says John Priestley at Barts and The London School of Medicine and Dentistry in London. However, a key question, Priestley points out, is whether the neurons are growing into the spinal cord at the other end. "Most previous scaffolds have supported axon growth into the scaffold but not out again. To achieve significant regeneration of spinal circuits, the scaffold must act as a bridge, not a cul-de-sac," he says.

Gelain says that fibres protruded a centimetre beyond the tubules, but without using special dye "tracers", he could not say whether they were native fibres growing in or regenerated ones growing out. "We will undertake these experiments soon," he says.

[http://www.eurekalert.org/pub\\_releases/2011-02/nocs-acv021111.php](http://www.eurekalert.org/pub_releases/2011-02/nocs-acv021111.php)

### **Arctic climate variation under ancient greenhouse conditions**

#### ***Tiny organisms preserved in marine sediments hold clues about Arctic climate variation during an ancient episode of greenhouse warming.***

Based on reconstructions of Arctic climate variability in the greenhouse world of the Late Cretaceous, Southampton scientists have concluded that man-made global warming probably would not greatly change the climatic influence associated with natural modes of inter-annual climate variability such as the El Niño – Southern Oscillation (ENSO) or the Arctic Oscillation/ North Atlantic Oscillation (AO/ NAO).

"Even in the warm Cretaceous period, the patterns of these climatic oscillations changed over longer decadal timescales," explained Professor Alan Kemp of the University of Southampton's School of Ocean and Earth Science based at the National Oceanography Centre, Southampton. "It is therefore difficult to predict whether anthropogenically driven warming will lead to systematic changes such as persistently milder European winters (a positive AO/ NAO) as some have suggested."

It is anticipated that the Arctic Ocean will become ice free during the summer within the next 15-50 years as a result of global warming. Because sea ice is reflective, its loss will reduce the amount of the Sun's energy bounced back out to space, thereby amplifying regional warming. However, changes in atmospheric circulation could also occur, making it difficult to unravel the likely net effect on climate.

"A key question is how an Arctic without permanent ice cover will affect atmospheric circulation and climate variability, particularly over high and mid latitudes," said Kemp.

One way of addressing this issue is to look back at previous greenhouse episodes in Earth's history. For example, Kemp's group has previously reported in the journal *Nature* that during the Late Cretaceous, when the dinosaurs roamed the world, the Arctic Ocean was free of ice in summer with only intermittent sea ice in the winter.

"Understanding Late Cretaceous climate should inform debate about future climate trends and variability under greenhouse conditions," said Kemp, whose team's new findings are published in *Geophysical Research Letters*.

In both studies, Kemp and his collaborators analysed sediment cores from a marine ridge in the Arctic Ocean. These sediments date to the Late Cretaceous (69-76 million years ago) and contain fossil remains of diatoms, an important group of phytoplankton – tiny planktonic marine plants.

The sediments contain alternating band-like laminae of two types, representing diatom growth conditions in the Arctic spring and summer, respectively. Each year is represented by a couplet of laminae, one of each type, which allowed the researchers to reconstruct ocean conditions at annual resolution.

"The presence of diatom laminae testify to ice-free Arctic summers during the Late Cretaceous, although there is also evidence of ice rafting by intermittent winter ice," said Kemp.

The researchers analysed two sections of sediment core covering between them a continuous period of around 1,000 years. By analysing the characteristics of the diatom laminae and measuring their thickness they were able to reconstruct climate-driven variation in ocean conditions both between years and over decades.

Their analyses revealed that the Arctic climate of the Late Cretaceous varied over various timescales with periodicities closely matching those observed in the modern Arctic. It therefore appears that the Arctic was subject to some of the same climatic influences in the Late Cretaceous as it is today, including ENSO, which periodically transmits equatorial influences to high-latitudes via ocean-atmosphere interactions.

"A modern Arctic lacking permanent sea ice should be subject to similar influences as it was under greenhouse conditions in the Late Cretaceous," said Kemp.

This is important because there has been an ongoing debate about whether natural modes of climate variability such as ENSO and AO/ NAO would be perturbed or enhanced by global warming caused by greenhouse gas emissions. Particular controversy has surrounded whether such warming could cause a permanent El Niño state or milder European winters.

"Based on our findings, it seems unlikely that man-made global warming would cause a permanent El Niño state," concluded Kemp.

*The researchers are Andrew Davies, Alan Kemp, and Heiko Pälike of the University of Southampton's School of Ocean and Earth Science based at the National Oceanography Centre, Southampton.*

*The research was funded by the Natural Environment Research Council.*

**Publications:**

*Davies, A., Kemp, A. E. S. & Pälike, H. Tropical ocean-atmosphere controls on inter-annual climate variability in the Cretaceous Arctic. Geophysical Research Letters 38, L03706, (011). doi:10.1029/2010GL046151*

*<http://www.agu.org/pubs/crossref/2011/2010GL046151.shtml>*

*Davies, A., Kemp, A. E. S. & Pyke, J. Late Cretaceous seasonal ocean variability from the Arctic. Nature 460, 254-258 (2009).*

*doi:10.1038/nature08141 <http://www.nature.com/nature/journal/v460/n7252/abs/nature08141.html>*

*[http://www.eurekalert.org/pub\\_releases/2011-02/uos-rmo021111.php](http://www.eurekalert.org/pub_releases/2011-02/uos-rmo021111.php)*

## **Researchers map out ice sheets shrinking during Ice Age**

***A set of maps created by the University of Sheffield have illustrated, for the first time, how our last British ice sheet shrunk during the Ice Age.***

Led by Professor Chris Clark from the University's Department of Geography, a team of experts developed the maps to understand what effect the current shrinking of ice sheets in parts of the Antarctic and Greenland will have on the speed of sea level rise.

The unique maps record the pattern and speed of shrinkage of the large ice sheet that covered the British Isles during the last Ice Age, approximately 20,000 years ago. The sheet, which subsumed most of Britain, Ireland and the North Sea, had an ice volume sufficient to raise global sea level by around 2.5 metres when it melted.

*These maps show the rate at which the ice sheet over the British Isles during the last Ice Age melted. The ka on the images is short for thousand years and BP is 'before present.' So 27 Ka BP is the map of the ice sheet at 27,000 years ago. University of Sheffield*

Using the maps, researchers will be able to understand the mechanisms and rate of change of ice sheet retreat, allowing them to make predictions for our polar regions, whose ice sheets appear to be melting as a result of temperature increases in the air and oceans.

The maps are based on new information on glacial landforms, such as moraines and drumlins, which were discovered using new technology such as remote sensing data that is able to image the land surface and seafloor at unprecedented resolutions. Experts combined this new information with that from fieldwork, some of it dating back to the nineteenth century, to produce the final maps of retreat.

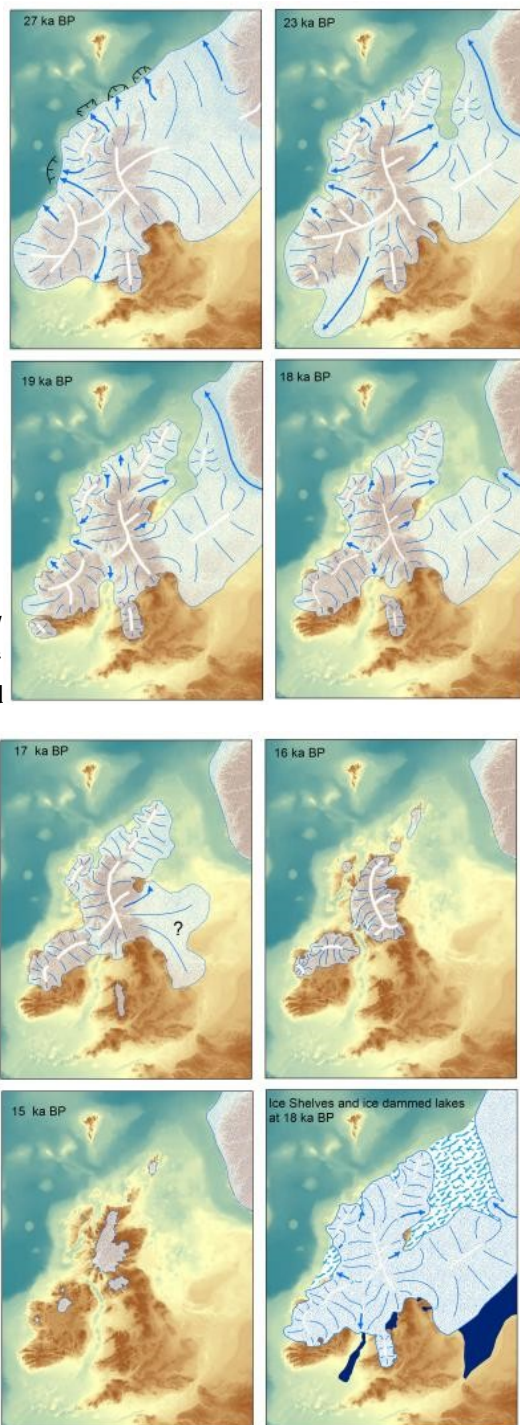
It is also possible to use the maps to reveal exactly when land became exposed from beneath the ice and was available for colonisation and use by plants, animals and humans. This provides the opportunity for viewers to pinpoint when their town/region emerged.

*These maps show the rate at which the ice sheet over the British Isles during the last Ice Age melted. The ka on the images is short for thousand years and BP is 'before present.' So 27 Ka BP is the map of the ice sheet at 27,000 years ago. University of Sheffield*

Professor Chris Clark, from the University of Sheffield's

Department of Geography, said: "It took us over 10 years to gather

all the information in order to produce these maps, and we are delighted with the results, It is great to be able to



visualise the ice sheet and notice that retreat speeds up and slows down, and it is vital of course that we learn exactly why. With such understanding we will be able to better predict ice losses in Greenland and Antarctica.

"In our next phase of work we hope to really tighten up on the timing and rates of retreat in more detail, by dropping tethered corers from a ship to extract seafloor sediments that can be radiocarbon dated."

*Notes for editors:* To receive the paper, published in *Quaternary Science Reviews*, please contact Shemina Davis, Media Relations Officer, on 0114 2225339 or email [shemina.davis@sheffield.ac.uk](mailto:shemina.davis@sheffield.ac.uk)

To view this news release and images online, visit <http://www.shef.ac.uk/mediacentre/2011/1842-ice-sheet-age-melt-maps.html>

[http://www.eurekalert.org/pub\\_releases/2011-02/jotn-fpr020911.php](http://www.eurekalert.org/pub_releases/2011-02/jotn-fpr020911.php)

### **Few physicians refer patients to cancer clinical trials**

***A small proportion of adult cancer patients participate in clinical trials in part due to a low level of physician referrals, according to an online study published Feb. 11 in The Journal of the National Cancer Institute.***

Although more than 8000 clinical trials are accepting participants, according to the National Cancer Institute (NCI), only an estimated 2% of newly diagnosed cancer patients participate in them. Prior studies suggest that most eligible patients do not enroll in trials because their physicians do not refer them.

To understand what types of physicians are referring their patients to clinical cancer trials, Carrie N. Klabunde, Ph.D., of NCI, and colleagues, conducted a survey-based study of specialty physicians caring for colorectal and lung cancer patients. The researchers analyzed data from the Cancer Care Outcomes Research and Surveillance Consortium (CanCORS) for 1533 oncologists, radiation oncologists, and surgeons caring for colorectal and lung cancer patients. The physicians had completed a survey during 2005.

The researchers found that 869 of the physicians, or 56.7%, responded that they had referred or enrolled at least one patient in clinical trials in the previous 12 months: 87.8% of medical oncologists, 66.1% of radiation oncologists, and 35% of surgeons. Two-thirds of the physicians affiliated with a Community Clinical Oncology Program or an NCI-designated cancer center reported participating in trials.

Furthermore, the researchers write, "Those more likely to participate in a clinical trial were medical or radiation oncologists (vs surgeons), were in larger practices, had academic appointments, saw a higher volume of lung or colorectal cancer patients, and attended weekly tumor board meetings."

The researchers also found that among the physicians who reported referring or enrolling at least one patient in cancer clinical trials in this period, the mean number of patients referred or enrolled was 17.2 for medical oncologists, 9.5 for radiation oncologists, and 12.2 for surgeons.

The researchers note that primary care physicians have limited involvement in discussing clinical trial participation with patients; and that financial incentives were associated with physicians' clinical trials accrual volume, a finding consistent with previous studies showing financial incentives influence physician behavior.

The researchers point out certain limitations of their study: the physicians surveyed do not comprise a nationally representative sample; the study is based on physicians' self-reports of their participation in clinical trials; and the measure of trials participation combined patient referral and enrollment.

The researchers conclude that continued monitoring of physician participation in cancer clinical trials is essential. They write, "More research is needed to better understand clinician attitudes toward clinical research and to examine specific features of practice infrastructure—including availability of support staff, electronic health records, reimbursement, and clinical trial databases—that facilitate or hinder physician participation in clinical trials."

In an accompanying editorial, Lori M. Minasian, M.D., and Ann M. O'Mara, M.D., of the Community Oncology and Prevention Trials Research Group at the National Cancer Institute (NCI), write that "the American public continues to value medical research," and cite a Mayo clinic study in which 76% of patients said they expected their treating physician to inform them about clinical trials.

The authors also point out that medical students will be required to learn about clinical and translational research, according to a new standard from the Liaison Committee on Medical Education.

The authors conclude: "If we want research to inform practice, we need a workforce of physicians who value the research and understand how to incorporate research results into their practice. Much of the American public looks to their physicians to do that." *Contact:* Article and editorial: [ncipressofficers@mail.nih.gov](mailto:ncipressofficers@mail.nih.gov); 301- 496-6641



## A plea for basic biology

By Holly Bik | Friday, February 11, 2011 | 3

***These days, science funding is like a cage fight—utterly brutal. It's even harder to compete for funding when you work on microscopic nematode worms that live at the bottom of the ocean.***

As an undergraduate at King's College London, I watched with great sadness as the university abolished departments—first chemistry, then biological sciences. At the time, the university blamed these closures on lackluster research portfolios and low interest from prospective students. I graduated in the penultimate biology class, as the university was shifting its focus towards its stronger, more highly rated biomedical programs.

Yet, at the time, I noticed great irony in my situation. As we heard more tales of our "underperforming" biology department, our lecturers were instead preaching about transformative discoveries fueled by basic biological research.

*Nematode image* by Dr. James Baldwin, Manuel Mundo and Tiago Pereira from the University of California Riverside.

In parasitology we learned that Artemisinins, some of the most potent and effective anti-malaria drugs, were originally discovered in an unremarkable pan-Eurasian herb, *Artemisia annua* (annual wormwood).

The overarching message of invertebrate zoology? Marine sponges are practically a gold mine.

The mere mention of this phylum elicits Pavlovian salivation from pharmaceutical companies—in addition to malaria, sponge chemicals are leading the fight against tumors, cancer, bacteria, inflammation, and arthritis. Even sponge skeletons have been tested as 'bioscaffolds' to help heal bone and cartilage injuries.

Some of the most revolutionary discoveries have origins in basic research—someone looking at an exotic, unusual plant (or even an overlooked, mundane plant), or studying species' weird adaptations to extreme environments like hot springs or the deep sea.

To harness nature's potential, humans need to know what's there. And what's there, for nematodes, is a big fat question mark. Nematodes may not offer us the cure for cancer, but they certainly have a story to tell.

In the wake of the Deepwater Horizon oil spill, our ecological ignorance and shocking lack of baseline information was certainly a wake up call. If only we knew what was there before, we could determine what damage has been done.

As a scientist, I have a natural curiosity and thirst for the minutiae, but I also realize the value of selling the big picture. In the Gulf of Mexico, assessing oil damage is now the biggest picture. In the U.S., the legal process of Natural Resource Damage Assessment (NRDA) is conducted by the government in the wake of environmental disasters—NRDA only covers damage to ecosystem services that affect humans: ecological, cultural, or historical impacts; commercial or recreational impacts; and passive value such as the preservation of wild spaces.

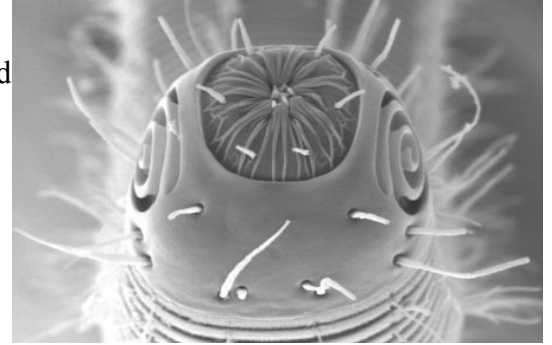
There are plenty of arguments: the NRDA process isn't fair, it is too cut and dry, it ignores the sacred chi of Mother Earth. But most NRDA officials I've spoken to are deeply passionate about science and lament the dearth of basic information needed for comprehensive damage assessments.

They're bound within a stringent legal framework—just like in court, companies like BP are innocent until there is definitive evidence of guilt. In the absence of published baseline studies, the default assumption is that no damage has occurred.

Out of context, you could argue that spending taxpayers' money on deep-sea worms is foolish and wasteful. But when you think about what happened in the Gulf of Mexico and consider what could be gained from understanding the earth's biodiversity, there really is no argument.

Funding slow, steady basic research may not always be considered "sexy science," but it may save lives. Literally.

*About the Author: Dr. Holly Bik is a postdoctoral researcher at the Hubbard Center for Genome Studies at the University of New Hampshire. Despite working in a genetics lab, she is marine biologist at heart—although occasionally she must convey enthusiasm for *C. elegans* in order to appease colleagues. Her current research uses high-throughput DNA sequencing to study marine meiofauna (microscopic animals such as nematode worms, protists and fungi) with a specific focus on the deep sea. Holly contributes to Deep-Sea News and is still trying to get the hang of Twitter @Dr\_Bik.*

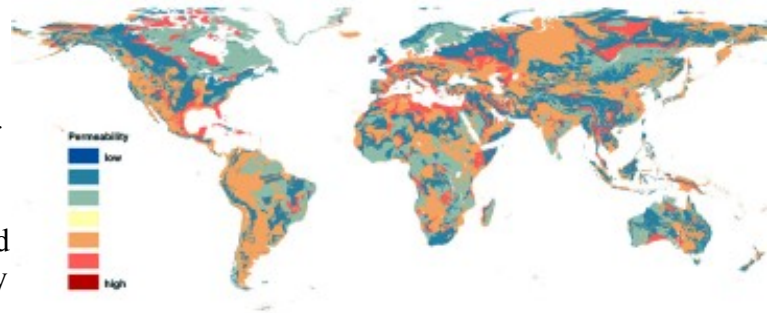




## First water map of Earth's leaky surface

**Michael Marshall, environment reporter**  
**See the first-ever global survey of Earth's permeability, showing which regions have rocks that water can pass through**

The map above ([click to enlarge](#)) is the first-ever global survey of Earth's permeability: essentially, how leaky it is. It shows how easily water passes through surface rocks, which will help us understand the planet's water cycle and predict the sustainability of underground water sources.



**Tom Gleeson/Geophysical Research Letters**

Crucially, it could help reveal the hidden underground movements of 99 per cent of unfrozen fresh water - water which is not taken into account in computer models used to predict the climate.

The map was put together by Tom Gleeson of the University of British Columbia in Vancouver, Canada, and his colleagues. They assembled data on the kinds of rocks found in different regions, and, using information on how permeable each type of rock is, calculated how leaky different regions are.

Permeability varies over 13 orders of magnitude, so the figures are not very precise, but they offer a rough picture. Gleeson says the map should help hydrologists to work out how much groundwater moves from one basin or aquifer to another, which is important if the water is to be managed sustainably.

At the moment we don't know how much water is hiding underground, or where it is. As a result, groundwater gets left out of climate models. Gleeson says that is a significant omission, as the movements of groundwater could well affect regional climate:

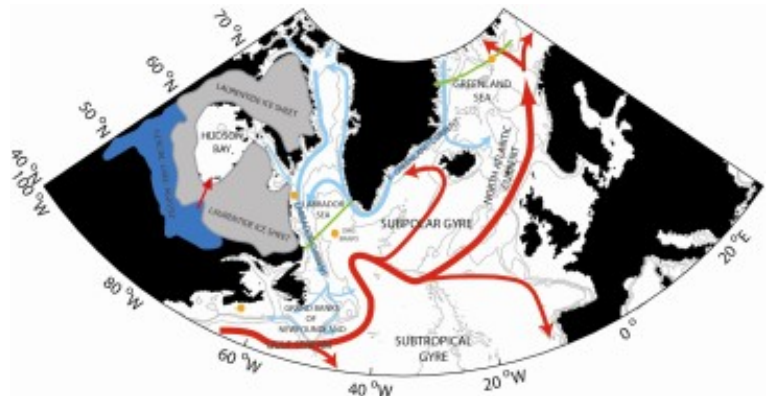
The map is a "very good first step", says Richard Taylor of University College London. However he says the figures for North America are the most reliable, because that area has been heavily studied, whereas those for the rest of the world are more scanty. *Journal reference: Geophysical Research Letters, DOI: 10.1029/2010GL045565*  
<http://www.newscientist.com/article/mg20927994.100-vacuum-has-friction-after-all.html>

## New model changes view of climate change

**(PhysOrg.com) -- Using new, high-resolution global ocean circulation models, University of Massachusetts Amherst geoscientist Alan Condron, with Peter Winsor at the University of Alaska, report this week that massive glacial meltwaters assumed to have flooded the entire North Atlantic 8,200 years ago, drastically cooling Europe, instead flowed thousands of miles further south.**

"These results dramatically affect our understanding of what causes climate change," Condron says.

The events unfolded when the Laurentide ice sheet, which covered much of Hudson Bay in Arctic Canada, gradually melted during a warm period about 8,200 years ago. The resulting glacial Lake Agassiz catastrophically broke through a kilometers-long ice dam at the bottom of the bay, suddenly dumping thousands of cubic kilometers of fresh water into the Atlantic Ocean.



[Enlarge](#)

Because this roughly coincided with the largest abrupt climate change recorded in the last 10,000 years, classic geoscience theory had assumed that the flood covered the surface of the Labrador and Greenland Seas and subpolar gyre with lighter, warmer and less salty water to trigger the cooling. Scientists have assumed this slowed the Gulf Stream and ocean convection by disrupting the Thermohaline circulation, that is, the large-scale temperature- and salt-driven ocean current responsible for our current warm, stable climate.

However, Condron and Winsor's new model, which is 10 to 20 times more powerful than previously attainable, suggests the freshwater flood of 8,200 years ago and others like it actually skirted past the subpolar gyre, instead traveling south by joining narrow, coast-hugging currents where water moves much faster than in the open ocean.

They summarize, "Using a high resolution, global, ocean-ice circulation model, we present an alternative view that freshwater discharged from glacial Lake Agassiz would have remained on the continental shelf as a narrow, buoyant, coastal current and would have been transported south into the subtropical North Atlantic."

If they're correct and fresh water from glacial Lake Agassiz did end up in the Gulf Stream much farther south, between 20 and 40 degrees of latitude in the subtropical gyre, it's revolutionary. "Basically, our model says that this flood ended up 3,000 miles further south than we all thought. It's observed at the same time as the climate change and cooling in Europe, but the picture is far more complicated and different than we'd assumed. We all thought it went much further north."

The new model runs on one of the world's top supercomputers at the National Energy Research Science Computing Center in Berkeley, Calif. "With this higher resolution modeling, our ability to capture near-shore boundary currents dramatically changes our idea of where the fresh water may be going. Lower-resolution models very much miss the complexity and detail that are now available in our high-res model," the authors say. Their findings appear in the current issue of *Geophysical Research Letters*.

Condron says the revised view is a result of much higher computational power available with faster computers. Older models weren't powerful enough to catch these subtleties because they contained too few data points to capture smaller-scale, faster-moving coastal currents. "We've shown that the conceptual idea in which flood waters once covered the subpolar gyre derives from the inability of lower resolution numerical models to accurately resolve narrow coastal flows, and is likely incorrect," he adds.

The new model is strengthened, Condron says, by present-day evidence that this coastally confined freshwater pathway is the same route taken by water flowing out of Hudson Bay now. Further, paleoceanographic evidence from the coastal shelf ocean supports this new view. "When we look offshore in the open ocean there really is very little evidence for this flood event, but there are clear sedimentary deposits from a large flood along the shelf."

"Our results are particularly relevant for how we model the melting of the Greenland and Antarctic ice sheets now and in the future. "It's apparent from our results that climate scientists are artificially introducing fresh water into their models much too far north, into parts of the ocean that it never would have reached. This has strong implications for predicting and understanding the stability of our future climate," says Condron. "We're in a similar interglacial period now, in the Holocene. The assumption is that the ocean looked and acted then much the same as it does today. So the coastal currents are assumed to be the same."

Their next step will be to understand the impact caused by this freshwater flooding into the subtropical, rather than the subpolar ocean to see if it may be related to cooling and climate disruption.

*Provided by University of Massachusetts Amherst*

<http://www.physorg.com/news/2011-02-compound-blocks-brain-cell-destruction.html>

### **Compound blocks brain cell destruction in Parkinson's disease**

***Scientists from the Florida campus of The Scripps Research Institute have produced the first known compound to show significant effectiveness in protecting brain cells directly affected by Parkinson's disease, a progressive and fatal neurodegenerative disorder.***

Although the findings were in animal models of the disease, the effectiveness of the compound, combined with its potential to be taken orally, offers the tantalizing possibility of a potentially useful future therapy for Parkinson's disease patients.

The results were published in two separate studies in the journal *ACS Chemical Neuroscience*.

"These studies present compelling data on the first oral, brain-penetrating inhibitor to show significant efficacy in preventing neurodegeneration in both mouse and rat models of Parkinson's disease," said team leader Philip LoGrasso, a professor in the Department of Molecular Therapeutics and senior director for drug discovery at Scripps Florida. "The compound offers one of the best opportunities we have for the development of an effective neuroprotective treatment."

The new small molecule—labeled SR-3306—is aimed at inhibiting a class of enzymes called c-jun-N-terminal kinases (JNK). Pronounced "junk," these enzymes have been shown to play an important role in neuron (nerve cell) survival. As such, they have become a highly viable target for drugs to treat neurodegenerative disorders such as Parkinson's disease.

"A drug like SR-3306 that prevents neurodegeneration would be a quantum leap in the clinical treatment of Parkinson's because all current therapies treat only the symptoms of the disease, not the underlying pathologies," LoGrasso said.

Patients with Parkinson's disease suffer from the loss of a group of neurons in the substantia nigra pars compacta (SNpc), part of the midbrain involved in motor control. These cells produce dopamine, a

neurotransmitter that plays a key role in motor reflexes and cognition. The disease also affects projecting nerve fibers in the striatum, a part of the forebrain filled with cells that interact with dopamine.

### **Stopping the Progression of Neuron Destruction in Animal Models**

The SR-3306 compound, which has been in development at Scripps Florida for several years, performed well in both cell culture and animal models. In cell culture, the compound showed greater than 90 percent protection against induced cell death of primary dopaminergic neurons, while in mouse models of induced neuron death, the compound showed protective levels of approximately 72 percent.

The scientists went one step further, testing the new compound in a rat model, which duplicates the physical symptoms often seen with the human disease—a pronounced and progressive loss of motor skills. The results showed SR-3306 provided a protection level of approximately 30 percent in the brain, a level that reduced the dysfunctional motor responses by nearly 90 percent.

"It was a surprise that level of neuroprotection reduced the behavioral impact so strongly," LoGrasso said, "but it's indicative of how it might perform in human patients. While SR-3306 doesn't represent a cure, it does appear to have the potential of stopping the progression of the disease."

The new studies are part of a \$7.6 million multiyear grant awarded to LoGrasso in 2008 by the National Institutes of Neurological Disorders and Stroke (NINDS). The grant will enable Scripps Research and potential partners to file an application for an investigational new drug (IND)—the first step in the lengthy clinical trials process required by the U.S. Food and Drug Administration before a new drug can be brought to market.

**More information:** "Small Molecule c-jun-N-terminal Kinase (JNK) Inhibitors Protect Dopaminergic Neurons in a Model of Parkinson's Disease," by Jeremy W. Chambers, Alok Pachori et al., <http://pubs.acs.org ... 21/cn100109k>

"JNK Inhibition Protects Dopamine Neurons and Provides Behavioral Improvement in a Rat 6-hydroxydopamine Model of Parkinson's Disease," by Candice E. Crocker et al., <http://pubs.acs.org ... 21/cn1001107> Provided by The Scripps Research Institute

[http://www.eurekalert.org/pub\\_releases/2011-02/nu-gaa021111.php](http://www.eurekalert.org/pub_releases/2011-02/nu-gaa021111.php)

### **Gonorrhea acquires a piece of human DNA**

#### **First evidence of gene transfer from human host to bacterial pathogen offers new view of evolution, disease**

CHICAGO --- If a human cell and a bacterial cell met at a speed-dating event, they would never be expected to exchange phone numbers, much less genetic material. In more scientific terms, a direct transfer of DNA has never been recorded from humans to bacteria.

Until now, Northwestern Medicine researchers have discovered the first evidence of a human DNA fragment in a bacterial genome – in this case, *Neisseria gonorrhoeae*, the bacterium that causes gonorrhea. Further research showed the gene transfer appears to be a recent evolutionary event.

The discovery offers insight into evolution as well as gonorrhea's nimble ability to continually adapt and survive in its human hosts. Gonorrhea, which is transmitted through sexual contact, is one of the oldest recorded diseases and one of a few exclusive to humans.

"This has evolutionary significance because it shows you can take broad evolutionary steps when you're able to acquire these pieces of DNA," said study senior author Hank Seifert, professor of microbiology and immunology at Northwestern University Feinberg School of Medicine. "The bacterium is getting a genetic sequence from the very host it's infecting. That could have far reaching implications as far as how the bacteria can adapt to the host."

It's known that gene transfer occurs between different bacteria and even between bacteria and yeast cells. "But human DNA to a bacterium is a very large jump," said lead author Mark Anderson, a postdoctoral fellow in microbiology. "This bacterium had to overcome several obstacles in order to acquire this DNA sequence."

The paper will be published Feb. 14 in the online journal mBio.

The finding suggests gonorrhea's ability to acquire DNA from its human host may enable it to develop new and different strains of itself. "But whether this particular event has provided an advantage for the gonorrhea bacterium, we don't know yet," Seifert said.

Every year an estimated 700,000 people in the United States and 50 million worldwide acquire gonorrhea. While the disease is curable with antibiotics, only one drug is now recommended for treatment because the disease developed resistance to previously used antibiotic options over the past four decades.

Gonorrhea is a particularly serious disease for women. If left untreated, gonorrhea can lead to pelvic inflammatory disease, a painful condition that can cause sterility and ectopic pregnancy. In rare cases, men and women can develop a form of the disease that leaves the genital tract and enters the bloodstream, causing arthritis and endocarditis, an infection of the inner lining of the heart.

An ancient disease that sounds like gonorrhea is described in the Bible, noted Seifert, who has studied the disease for 28 years. Most of his research focuses on how the bacterium evades the human immune system by altering its appearance and modulating the action of white blood cells.

The gene transfer was discovered when the genomic sequences of several gonorrhea clinical isolates were determined at the Broad Institute in Cambridge, Mass. Three of the 14 isolates had a piece of DNA where the sequence of DNA bases (A's, T's, C's and G's) was identical to an L1 DNA element found in humans.

In Seifert's Feinberg lab, Anderson sequenced the fragment to reconfirm it was indeed identical to the human one. He also showed that this human sequence is present in about 11 percent of the screened gonorrhea isolates.

Anderson also screened the bacterium that causes meningitis, *Neisseria meningitidis*, and is very closely related to gonorrhea bacteria at the genetic level. There was no sign of the human fragment, suggesting the gene transfer is a recent evolutionary event.

"The next step is to figure out what this piece of DNA is doing," Seifert said.

*The research was sponsored by the National Institutes of Health.*