Psychopaths' brains wired to seek rewards, no matter the consequences

The brains of psychopaths appear to be wired to keep seeking a reward at any cost, new research from Vanderbilt University finds. The research uncovers the role of the brain's reward system in psychopathy and opens a new area of study for understanding what drives these individuals.

The results were published March 14, 2010, in Nature Neuroscience.

"Psychopaths are often thought of as cold-blooded criminals who take what they want without thinking about consequences," Joshua Buckholtz, a graduate student in the Department of Psychology and lead author of the new study, said. "We found that a hyper-reactive dopamine reward system may be the foundation for some of the most problematic behaviors associated with psychopathy, such as violent crime, recidivism and substance abuse."

Previous research on psychopathy has focused on what these individuals lack - fear, empathy and interpersonal skills. The new research, however, examines what they have in abundance - impulsivity, heightened attraction to rewards and risk taking. Importantly, it is these latter traits that are most closely linked with the violent and criminal aspects of psychopathy.

"There has been a long tradition of research on psychopathy that has focused on the lack of sensitivity to punishment and a lack of fear, but those traits are not particularly good predictors of violence or criminal behavior," David Zald, associate professor of psychology and of psychiatry and co-author of the study, said. "Our data is suggesting that something might be happening on the other side of things. These individuals appear to have such a strong draw to reward - to the carrot - that it overwhelms the sense of risk or concern about the stick."

To examine the relationship between dopamine and psychopathy, the researchers used positron emission tomography, or PET, imaging of the brain to measure dopamine release, in concert with a functional magnetic imaging, or fMRI, probe of the brain's reward system.

"The really striking thing is with these two very different techniques we saw a very similar pattern - both were heightened in individuals with psychopathic traits," Zald said.

Study volunteers were given a personality test to determine their level of psychopathic traits. These traits exist on a spectrum, with violent criminals falling at the extreme end of the spectrum. However, a normally functioning person can also have the traits, which include manipulativeness, egocentricity, aggression and risk taking.

In the first portion of the experiment, the researchers gave the volunteers a dose of amphetamine, or speed, and then scanned their brains using PET to view dopamine release in response to the stimulant. Substance abuse has been shown in the past to be associated with alterations in dopamine responses. Psychopathy is strongly associated with substance abuse.

"Our hypothesis was that psychopathic traits are also linked to dysfunction in dopamine reward circuitry," Buckholtz said. "Consistent with what we thought, we found people with high levels of psychopathic traits had almost four times the amount of dopamine released in response to amphetamine."

In the second portion of the experiment, the research subjects were told they would receive a monetary reward for completing a simple task. Their brains were scanned with fMRI while they were performing the task. The researchers found in those individuals with elevated psychopathic traits the dopamine reward area of the brain, the nucleus accumbens, was much more active while they were anticipating the monetary reward than in the other volunteers.

"It may be that because of these exaggerated dopamine responses, once they focus on the chance to get a reward, psychopaths are unable to alter their attention until they get what they're after," Buckholtz said. Added Zald, "It's not just that they don't appreciate the potential threat, but that the anticipation or motivation for reward overwhelms those concerns." *The National Institute on Drug Abuse funded the research.*

Zald is an investigator in the Vanderbilt Kennedy Center for Research on Human Development.

Medieval Child's Brain Found Preserved

Scientists were able to identify neurons and cerebral cells from the brain preserved from the 13th century.

By Rossella Lorenzi Mon Mar 15, 2010 04:54 AM ET

THE GIST:

**** Intact neurons and cells were identified within an 18-month-old child's brain from the 13th century.***

**** The remains were found in northwestern France where salty clay soil and fresh and briny water all worked to naturally preserve the brain.***

**** The find reveals how well human brain cells can potentially survive the centuries.***

An international team of researchers has identified intact neurons and cerebral cells in a mummified medieval brain, according to a study published in the journal Neuroimage.

Found inside the skull of a 13th century A.D. 18-month-old child from northwestern France, the brain had been fixed in formalin solution since its discovery in 1998.

"Although reduced by about 80 percent of its original weight, it has retained its anatomical characteristics and most of all, to a certain degree its cell structures," anatomist and palaeopathologist Frank Ruhli, head of the Swiss Mummy Project at the University of Zurich, Switzerland, told Discovery News.

This brain was found inside the skull of a 13th century A.D. 18-month-old child from northwestern France.
Heinz Sonderegger, Institute of Anatomy, University of Zurich

The brain was the only tissue preserved in the infant's skeletonized body. "It is a unique case of naturally-occurring preservation of human brain tissue in the absence of other soft tissues," Ruhli said.

The brain appeared almost intact. The grooves and furrows - gyri and sulci - that make up the surface of the brain's cerebral cortex were still clearly visible, as well the frontal, temporal and occipital lobe.

Amazingly, the cellular structure had also been preserved to a certain degree. Microscopic examination of the tissue revealed gray and white matter, blood vessels and large neurons near the hippocampus area, the memory-making region of the brain. The cells had mostly retained their original shape as well as the dendrites, the short, branched fibers that extend from the cell body of a neuron.

"It is an exceptional find, as cell structures are identified in preserved ancient cerebral tissues," Ruhli said.

Indeed, soft tissue decomposition and brain removal as part of the embalming process in most anthropogenic mummies, make it extremely difficult to even find preserved cerebral tissues from archaeological human remains.

According to the researchers, the amazing preservation of the medieval brain occurred because of the burial's peculiar location. Wrapped in a leather envelope inside a wooden coffin, with a pillow under the head, the infant was exhumed in Quimper-Bretagne, France. Here acidic clay soil and fresh and briny water (the city lies at the confluence of three rivers amid Atlantic tides) basically preserved the brain like a pickle.

"It's called adipocere and is the result of a chemical reaction. In the presence of bacterial enzymes, body fats react with water and hydrogen and produce a soap-like substance able to slow down or inhibit decomposition," Christina Papageorgopoulou, first author of the study, told Discovery News.

The researchers also investigated the possible cause of death of the infant, dismissing a previous diagnosis of a cerebral hemorrhage.

"Heavy bleeding occurred on the outer surface of the cortex at least several days before the child's death. This is evidence of a skull fracture. Whether it is the cause of death, we can't say for sure," Raffaella Bianucci, an anthropologist in the Department of Animal and Human Biology at the University of Turin, said.

According to Maciej Henneberg, professor of anthropological and comparative anatomy at the University of Adelaide, the study is important as an investigations into the evolution of brain morphology and pathology.

"It shows that cell structures can survive for a long time," Henneberg told Discovery News.

Vertebroplasty for patients with osteoporosis provides effective pain relief

For best results, patient selection, correct indications, optimal medical treatment needed, according to a study of nearly 1,500 patients over seven years

TAMPA, Fla. - Patient selection is key for vertebroplasty—a minimally invasive treatment performed by interventional radiologists in individuals with painful osteoporotic vertebral compression fractures that fail to respond to conventional medical therapy—to be effective and successful, according to a study of more than 1,500 persons who were followed over seven years. Additionally, collaboration between an interventional radiologist and other medical experts in treating a patient is imperative, say researchers at the Society of Interventional Radiology's 35th Annual Scientific Meeting in Tampa, Fla.

"Vertebroplasty puts lives and vertebrae back together," said Giovanni C. Anselmetti, M.D., interventional radiologist at the Institute for Cancer Research and Treatment in Turin, Italy. Before treatment, many osteoporotic patients are in constant pain and cannot manage everyday activities. Vertebroplasty, a minimally invasive treatment performed by interventional radiologists under imaging guidance, stabilizes collapsed vertebrae with the injection of medical-grade bone cement into the spine. The treatment provides pain relief and improves one's quality of life—if given to appropriately selected candidates in whom conventional medical treatment has failed (such as analgesics or narcotic drugs that provide minimal or no pain release or doses that

are intolerable), he further explained. "Our long-term follow-up confirmed this: pain relief and quality of life significantly improved with vertebroplasty," said Anselmetti.

Osteoporosis, the most common type of bone disease, is characterized by low bone mass and structural deterioration of the bone, resulting in an increased susceptibility to fractures. Osteoporosis affects 10 million Americans and is responsible for 700,000 vertebral fractures each year. Multiple vertebral fractures can result in chronic pain and disability, loss of independence, stooped posture and compression of the lungs and stomach.

"Vertebroplasty dramatically improves back pain within hours of the procedure, provides long-term pain relief and has a low complication rate, as demonstrated in multiple studies," said Anselmetti. Vertebroplasty provides pain relief from the complications of osteoporosis (vertebral fractures) but not the disease that caused it (osteoporosis), said Anselmetti. "For the best results, collaboration between physicians is mandatory. All osteoporotic patients need to be followed by an interventional radiologist, who determines which patients are appropriate candidates to receive vertebroplasty treatment, and an experienced medical expert (in this study, a rheumatologist) to ensure continued treatment for osteoporosis," he said.

Anselmetti illustrated a typical case: an 80-year-old Italian woman, who was diagnosed last year with two painful osteoporotic vertebral collapses, underwent medical treatment for osteoporosis (with the drug teriparatide) and was still in pain when she was prescribed an external brace. After there was evidence of two new fractures (verified by MR imaging), she received vertebroplasty, experiencing "complete pain regression, no need for the brace and a dramatic Lazarus-like ability to perform daily activities," he noted.

Researchers studied 2,251 osteoporotic patients (1,811 women; average age, 65) suffering from back-pain for vertebral collapses (MRI confirmed) who underwent a clinical interview; their medical treatment, pain grade, quality of life and extent of vertebral fracture were reviewed. Vertebroplasty was performed in 1,542 patients (1,302 women; average age, 73) when optimal medical treatment (such as biphosphonates, teriparatide, analgesics and back brace) did not help relieve pain or improve quality of life for patients over a three-month period. After vertebroplasty, patients continued to receive medical treatment with a rheumatologist. Because interventional radiologists use high-quality, image-guiding systems (such as digital flat-panel fluoroscopy with built-in rotational image acquisition), treatment time is decreased, making for a safer procedure, added Anselmetti.

In 1,494 patients (96.9 percent), the average pretreatment pain score on the 11-point visual analog scale was 8.2±1.8, and it dropped "significantly" to an average of 1.1±1.6 after vertebroplasty treatment, said Anselmetti. A patient's ability to manage everyday life—such as washing, dressing or standing—was measured by the commonly used Oswestry Disability Questionnaire, which was completed by patients before and after vertebroplasty. The ODQ scores changed from an average of 68.7±7.6 percent to 18.5±8.2 percent. Long-term follow-up (average, 31.2 months) in 1,017 patients (857 women; average age, 72) showed the VAS significantly dropping from 7.9±1.5 to 1.3±1.7. Of the 757 patients wearing a back brace before vertebroplasty, 683 could stop wearing one after treatment.

Anselmetti said that additional studies need to be performed, such as a large randomized trial comparing conventional medical treatment to medical treatment plus vertebroplasty. In Europe, this is difficult, as patients with chronic back pain for vertebral osteoporotic fractures prefer to be treated by vertebroplasty - and not randomized into a medical treatment-only group. "Patients who are in so much pain ask if they can be considered for vertebroplasty treatment," said the co-author of "Percutaneous Vertebroplasty (PV) in the Osteoporotic Patients: Optimal Indications and Patient Selection to Improve Clinical Outcome: Personal Experience in 1,542 Patients Over Seven Years' Experience."

More information about the Society of Interventional Radiology, interventional radiologists and vertebroplasty can be found online at www.SIRweb.org.

Abstract 16: "Percutaneous Vertebroplasty (PV) in the Osteoporotic Patients: Optimal Indications and Patient Selection to Improve Clinical Outcome: Personal Experience in 1,542 Patients Over Seven Years' Experience," G.C. Anselmetti, A. Manca, G. Chiara, G. Iussich and D. Regge, all at the Institute for Cancer Research and Treatment, Candiolo, Italy; and G. Isaia, University of Turin, Turin, Italy, SIR 35th Annual Scientific Meeting March 13, 2010, Tampa, Fla. This abstract can be found at www.SIRmeeting.org.

Electronics 'missing link' brings neural computing closer

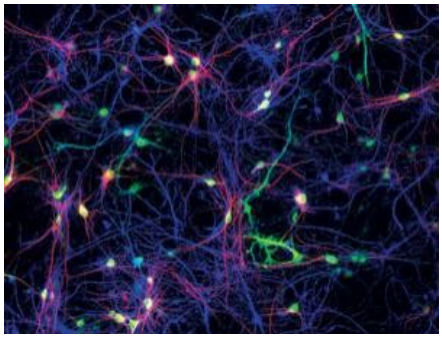
* 15 March 2010 **by Paul Marks**

WHEN the "missing link of electronics" was finally built in 2008, it was the vindication of a 30-year-old prediction. Now it seems the so-called memristor can behave uncannily like the junctions between neurons in the brain.

A memristor is a device that, like a resistor, opposes the passage of current. But memristors also have a memory. The resistance of a memristor at any moment depends on the last voltage it experienced, so its behaviour can be used to recall past voltages.

Now memristors are being used in a US military-funded project trying to make brain-like computers, says Wei Lu, who led the team at the University of Michigan in Ann Arbor that demonstrated the new behaviour (Nano Letters, DOI: 10.1021/nl904092h).

The memristor's existence was predicted in 1971, when Leon Chua of the University of California, Berkeley, spotted a gap in the capabilities of basic electrical components. But it was not until 2008 that Stanley Williams at Hewlett-Packard Labs in Palo Alto, California, made the first memristor from a speck of titanium dioxide, the pigment in most white paint.



Coming soon to a CPU near you **Patrick Landmann/SPL**

The race to use memristors in computing has been on ever since, with brain-like computers one of the potential applications (New Scientist, 4 July 2009, p 42). Memristors lend themselves to the task because the way that their resistance gives a glimpse of an earlier voltage is analogous to the way that a synapse's electrical behaviour is dependent on its past activity.

Lu and colleagues have now provided the first demonstration that the analogy stands up. What's more, their memristors were built with materials already used in the manufacture of computer chips.

Lu's team used a mixture of silicon and silver to join two metal electrodes where they cross. The junction mimics a particular behaviour of synapses that allows neurons to learn new firing patterns, and is believed to allow memories to be stored.

In the brain the timing of electrical signals in two neurons affects the ease with which later messages can jump across the synapse between them. If the pair fire in close succession, the synapse becomes more likely to pass subsequent messages between the two. "Cells that fire together, wire together," says Lu.

The Michigan device exhibits the same behaviour. When the gap between signals on the two electrodes was 20 milliseconds, the resistance to current flowing between the two was roughly half that after signals separated by 40 milliseconds. "The memristor mimics synaptic action," says Lu, adding that the next step will be to build circuits with tens of thousands of memristor synapses.

Williams is pleased the long-predicted component is showing potential. "I am glad to see that our work is having an influence," he told New Scientist.

Studies find treating vitamin D deficiency significantly reduces heart disease risk

Preventing and treating heart disease in some patients could be as simple as supplementing their diet with extra vitamin D, according to two new studies

Preventing and treating heart disease in some patients could be as simple as supplementing their diet with extra vitamin D, according to two new studies at the Intermountain Medical Center Heart Institute in Murray, Utah. Researchers at the Intermountain Medical Center Heart Institute last fall demonstrated the link between vitamin D deficiency and increased risk for coronary artery disease. These new studies show that treating vitamin D deficiency with supplements may help to prevent or reduce a person's risk for cardiovascular disease and a host of other chronic conditions. They also establish what level of vitamin D further enhances that risk reduction. *Study findings will be presented at the American College of Cardiology 59th annual scientific session in Atlanta at 3:30 pm, EST, on March 15, 2010. PLEASE NOTE EMBARGO REQUIREMENTS.*

"Vitamin D replacement therapy has long been associated with reducing the risk of fractures and diseases of the bone," says Dr. J. Brent Muhlestein, MD, director of cardiovascular research at the Intermountain Medical Center Heart Institute. "But our findings show that vitamin D could have far greater implications in the treatment and reduction of cardiovascular disease and other chronic conditions than we previously thought."

For the first study, researchers followed two groups of patients for an average of one year each. In the first study group, over 9,400 patients, mostly female, reported low initial vitamin D levels, and had at least one follow up exam during that time period. Researchers found that 47 percent of the patients who increased their levels of vitamin D between the two visits showed a reduced risk for cardiovascular disease.

In the second study, researchers placed over 31,000 patients into three categories based on their levels of vitamin D. The patients in each category who increased their vitamin D levels to 43 nanograms per milliliter of blood or higher had lower rates of death, diabetes, cardiovascular disease, myocardial infarction, heart failure, high blood pressure, depression, and kidney failure. Currently, a level of 30 nanograms per milliliter is considered "normal."

Heidi May, PhD, a cardiovascular clinical epidemiologist with the Intermountain Medical Center Heart Institute, and one of the study's authors, says the link between low levels of vitamin D and increased risk for a variety of diseases is significant.

"It was very important to discover that the 'normal' levels are too low. Giving physicians a higher level to look for gives them one more tool in identifying patients at-risk and offering them better treatment," says Dr. May.

Dr. Muhlestein says the results of these studies will change the way he treats his patients.

"Although randomized trials would be useful and are coming, I feel there is enough information here for me to start treatment based on these findings," he says.

Treatment options in this case are simple, starting with a blood test to determine a patient's vitamin D level. If low levels are detected, supplements and/or increased exposure to sunlight may be prescribed.

Increasing vitamin D intake by 1000 to 5000 international units (IU) a day may be appropriate, depending on a patient's health and genetic risk, says Dr. Muhlestein. He says supplements are the best source of vitamin D because they are relatively inexpensive and can be found at almost any supermarket or drug store. Most supplements provide an average of 400 IU per tablet.

While exposure to 20-30 minutes of sunlight can provide up to 10,000 IU, Dr. Muhlestein says it is important to use sunscreen and avoid the hottest parts of the day in order to avoid sunburn and the harmful UV rays associated with skin cancer.

Meat-Eating Amphibian Predated Dinos

A newly found bumpy-skinned, terrestrial amphibian lived 70 million years before dinosaurs in what is now Pennsylvania.

By Jennifer Viegas Mon Mar 15, 2010 02:00 PM ET

THE GIST:

**** A skull found at a FedEx site near Pittsburgh International Airport belonged to a meat-eating amphibian.***

**** The carnivorous amphibian lived 70 million years before the first dinosaurs emerged.***

**** Although the amphibian became extinct, it belonged to a superfamily that may have given rise to modern amphibians.***

Fedexia hunting in the The Age of Amphibians, some 300 million years ago, in what is now Pennsylvania.
Reconstruction: Mark A. Klingler/Carnegie Museum of Natural History

An interesting "rock" initially tossed aside at a FedEx site near Pittsburgh International Airport turns out to be the skull of a meat-eating, early terrestrial amphibian that lived 70 million years before the first dinosaurs emerged, according to a paper released today in Annals of Carnegie Museum.

The approximately 300-million-year-old carnivorous amphibian has been named Fedexia striegeli, after the well-known shipping service and Adam Striegel, who spotted the animal's well-preserved, five-inch-long fossil skull while he was a University of Pittsburgh student on a field trip.

Striegel originally threw it aside, thinking it wasn't important, but then he and class lecturer Charles Jones noticed pointy teeth and tusks, so the skull was brought to experts at the Carnegie Museum of Natural History.

"Fedexia might have resembled, using modern analogies, an overgrown or giant newt salamander about 2 feet long, including the tail, with a coarse, granular skin texture," co-author David Berman, curator of vertebrate paleontology at the museum, told Discovery News.

The graininess probably resulted from rice-sized bony elements, which were found on a close relative of this species from New Mexico, Anconastes vesperus, which Berman and other colleagues discovered. He said the protrusions "undoubtedly protected it from physical injuries from either predators or inanimate obstacles in the environment, and loss of body moisture through the skin, which modern amphibians are susceptible to."

He added that the carnivore's "large palatal tusks were undoubtedly formidable weapons for holding onto, crushing and dismembering prey" that likely included everything from smaller amphibians to large insects.

Analysis of the skull determined that Fedexia belongs to an extinct group of amphibians called Trematopidae. The trematopids provide the first evidence for North American vertebrate life that was adapted to a mostly terrestrial existence.

Co-author David Brezinski, an associate curator in the Section of Invertebrate Paleontology at the museum, explained to Discovery News that the toothy land-dweller lived when Earth's climate was in a period of radical transition.

Pennsylvania then was in the tropics and experienced a lot of rain during the Late Paleozoic Ice Age starting at around 320 million years ago. This helped to fuel plant growth.

"The increased rainfall, and attendant wet conditions were perfect for amphibians," Brezinski said. "That is, until things temporarily began drying out at about 304 million years ago."

The preceding period when moist conditions flourished led to what is now called the "Age of Amphibians," when the ancestors of Fedexia and other amphibians were a dominant group in Western Pennsylvania and other regions. The loss of water during the dry out, however, forced many of these animals, like Fedexia, to shift from a mainly aquatic to a mostly terrestrial existence.

"Amphibians that could exist for protracted times out of water should have been selected for," Brezinski said.

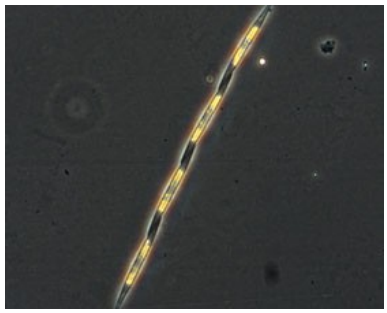
Relatives of Fedexia dating to 20 million years after its lifetime have been found at other sites, suggesting that this group successfully expanded and diversified even as the tropics became drier. He and his colleagues believe that these very early land-adapted amphibians only returned to the water perhaps to mate or lay eggs.

Although the Trematopidae eventually died out, they were part of a superfamily called Dissorphoidea that, Berman said, "are often hypothesized as possible ancestors of modern amphibians."

Ocean Geoengineering Scheme May Prove Lethal

Seeding the oceans with iron could result in the production of a potent neurotoxin, putting the lives of birds, fish and even humans at risk.

By Jessica Marshall Mon Mar 15, 2010 03:01 PM ET



THE GIST:

**** One type of phytoplankton that feeds on iron could sequester carbon, but may also produce a potent neurotoxin.***

**** The neurotoxin can and has killed or weakened fish, birds and people.***

**** Other geoengineering schemes may have similar, unintended consequences.***

Although phytoplankton may prove an unlikely ally in the effort to reduce the impact of climate change, enlisting these microorganisms to sequester carbon could have deadly consequences.

Proposals to use large-scale iron fertilization to combat climate change have been met with concern about the unintended consequences they could bring. **New Jersey Department of Environmental Protection**

One proposed method to combat climate change is to dump iron in regions of the ocean where the growth of marine phytoplankton -- tiny organisms that grow via CO2-absorbing photosynthesis -- is limited by the amount of iron available.

Adding iron is intended to cause a bloom of phytoplankton growth, sucking up CO2 in the process.

But new findings, published today in the Proceedings of the National Academy of Sciences, show that one type of phytoplankton that thrives under such circumstances makes domoic acid, a potent neurotoxin. This neurotoxin can move up the food chain as other animals eat the phytoplankton, harming sea life. The toxin can kill or weaken birds, fish, sea mammals or even humans who eat seafood that contains the toxin.

In coastal waters, blooms of Pseudonitzschia, the organism that produces the toxin, have occasionally closed coastal shellfish harvests. In a few instances, people have died from consuming contaminated seafood.

Coastal waters typically contain much more iron, which encourages Pseudonitzschia's growth, said Charles Trick of the University of Western Ontario, who led the new study.

The researchers gathered samples of seawater from the eastern Pacific during an expedition designed to test the effect of adding iron to the ocean to stimulate plankton growth. They added extra iron to the seawater samples on board their ship and measured the amount of neurotoxin that was produced and what kind of phytoplankton grew.

"If we added the normal amount of iron that one would add for these fertilization experiments, the level of toxins in each of the cells goes higher," Trick said. "It allows (Pseudonitzschia) to grow faster. And as they grow, they stop the other species from growing. They become dominant."

"The surprising part was not just that it made toxin," Trick said, "but that it made lots of toxin, and it stopped the other species from getting the nutrients."

Proposals to use large-scale iron fertilization to combat climate change have been met with concern about the unintended consequences they could bring.

One company that had hoped to sell carbon offsets by seeding the ocean with plankton, Planktos, has put its efforts on hold. But other companies are still pursuing the possibility, said Kenneth Coale of the Moss Landing Marine Laboratory in Moss Landing, Calif.

"We too have measured domoic acid production in our enrichment experiments, but find a much larger response than those reported by Trick et al.," Coale said. "Together these results suggest a wrinkle in the notion that iron fertilization could simply draw down atmospheric carbon dioxide. Nature is always more complex, and the curve she has thrown us needs to be carefully considered before iron fertilization should be seriously considered as a carbon sequestration option."

"Now we've dealt with one of the uncertainties, and we recognize that we don't know as much as we think," Trick agreed. "Modifications of nature at this big scale are kind of a fickle process. We'd like to think that we're smart enough to understand exactly what's going to happen. But in reality, the possibility that something unsuspected like this could happen is large, and we might not want to take that risk."

"That's one of the concerns with all of these geoengineering schemes," said Mak Saito of the Woods Hole Oceanographic Institution in Woods Hole, Mass. "If we're going to actively change the planet's chemistry or biology to actively reverse global warming, what are the unintended consequences? Here he's already documented one of the concerns. What are the ones we don't even know about?"

"None of these strategies will really be effective without conservation and reduction of carbon dioxide emissions," Saito added. "I kind of see them as weapons of last resort. To what extent are we on a trajectory that is so bad that we have to use these, and at what point do we say we have to accept these consequences?"

Erectile dysfunction strong predictor of death, cardiovascular outcomes

Study Highlights:

**** Men with cardiovascular disease and erectile dysfunction (ED) are at higher risk for death from all causes and also are more likely to suffer cardiovascular death, heart attack, stroke and heart failure hospitalization.***

**** Treatments effective in reducing cardiovascular disease had no effect on ED.***

**** Erectile dysfunction should be considered a risk factor for cardiovascular disease, researchers said.***

DALLAS Erectile dysfunction (ED) is a strong predictor of death from all causes and of heart attack, stroke and heart failure in men with cardiovascular disease (CVD), German researchers reported in Circulation: Journal of the American Heart Association.

In the first study to show that ED is predictive of death and cardiovascular outcomes, researchers found that men with CVD and ED (compared to those without ED) were twice as likely to suffer death from all causes and 1.6 times more likely to suffer the composite of cardiovascular death, heart attack, stroke and heart failure hospitalization. More specifically, they were:

* 1.9 times more likely to die from cardiovascular disease;
* twice as likely to have a heart attack;
* 1.2 times more likely to be hospitalized for heart failure; and
* 1.1 times more likely to have a stroke.

The researchers also found that, though ACE inhibitors, angiotensin receptor blockers or a combination of the two, can reduce cardiovascular events in high-risk patients, the medications didn't influence the course nor the development of ED.

"Erectile dysfunction is something that regularly should be addressed in the medical history of patients; it might be a symptom of early atherosclerosis," said Michael Böhm, M.D., lead author of the study and chairman of internal medicine in the Department of Cardiology and Intensive Care at the University of Saarland, Germany.

The worldwide study included 1,519 men from 13 countries in a substudy of the ONTARGET and TRANSCEND trials of cardiovascular patients. The men answered a questionnaire to determine whether they had ED. Men with ED were then categorized as having mild, mild-to-moderate, moderate or severe ED. The questionnaires were given at the initial visit, after two years or at the final visit after an average follow-up of five years.

ONTARGET patients were either randomly assigned to the ACE inhibitor drug ramipril (400 patients), telmisartan (395 patients) or a combination (381 patients). In TRANSCEND, researchers randomized ACE inhibitor-intolerant patients to placebo (202 patients) or telmisartan (171 patients).

The researchers found that patients with ED were older, and had a higher prevalence of hypertension, stroke, diabetes and lower urinary tract surgery than those without ED. Furthermore, 55 percent of the men had ED at entry in the trials. Deaths from all causes occurred in 11.3 percent of the patients who reported ED at baseline, but in only 5.6 percent of those with no or mild ED at the start of the study. The composite primary outcome of cardiovascular death, heart attack, stroke and heart failure hospitalization occurred in 16.2 percent of ED patients compared to 10.3 percent of patients with no or mild ED.

The risks of death from all causes and composite outcome increased in a stepwise manner with the progression of ED, researchers said. It is likely that the presence of ED identified individuals whose cardiovascular disease might be far more advanced than when evaluated with other clinical parameters alone," Böhm said.

ED is closely associated with the endothelial dysfunction that occurs in atherosclerosis and the vascular disturbances such as the build-up of plaque that precedes events such as heart attack and stroke, Böhm said.

"Men with ED going to a general practitioner or a urologist need to be referred for a cardiology workup to determine existing cardiovascular disease and proper treatment," Böhm said. "ED is an early predictor of cardiovascular disease."

Many men with ED see a general practitioner or a urologist to get medication for ED, he said.

"The medication works and the patient doesn't show up anymore," Böhm said. "These men are being treated for the ED, but not the underlying cardiovascular disease. A whole segment of men is being placed at risk."

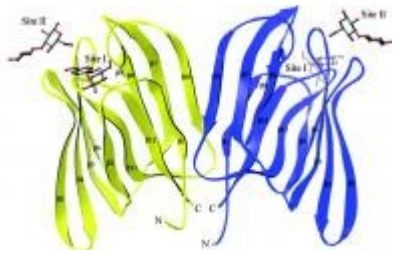
Men need to consider ED as a risk factor for cardiovascular disease just as high blood pressure and cholesterol are, Böhm said. "If a man has erectile dysfunction, then he needs to ask his physician to check for other risk factors of cardiovascular disease."

Co-authors are: Magnus Baumhakel, M.D.; Koon Teo, M.B., Ph.D.; Peter Sleight, M.D.; Jeffrey Probstfield, M.D.; Peggy Gao, M.Sc.; Johannes F. Mann, M.D.; Rafael Diaz, M.D.; Gilles R. Dagenais, M.D.; Garry L.R. Jennings, M.D.; Lisheng Liu, M.D.; Petr Jansky, M.D. and Salim Yusuf, M.B., B.S. Author disclosures are on the manuscript.
Boehringer-Ingelheim, Germany funded the substudy.

University of Michigan scientists identify chemical in bananas as potent inhibitor of HIV infection

Discovery of how BanLec binds to key HIV-1 protein opens door to developing microcides that can prevent sexual transmission of HIV

ANN ARBOR, Mich. – A potent new inhibitor of HIV, derived from bananas, may open the door to new treatments to prevent sexual transmission of HIV, according to a University of Michigan Medical School study published this week.



This is a 3-D structure of BanLec, a chemical isolated from bananas identified as a potent new inhibitor of HIV infection. **University of Michigan Medical School**

Scientists have an emerging interest in lectins, naturally occurring chemicals in plants, because of their ability to halt the chain of reaction that leads to a variety of infections.

In laboratory tests, BanLec, the lectin found in bananas, was as potent as two current anti-HIV drugs. Based on the findings published March 19 in the Journal of Biological Chemistry, BanLec may become a less expensive new component of applied vaginal microbicides, researchers say.

New ways of stopping the spread of the HIV are vitally needed. The rate of new infections of HIV is outpacing the rate of new individuals getting anti-retroviral drugs by 2.5 to1, and at present it appears an effective vaccine is years away. "HIV is still rampant in the U.S. and the explosion in poorer countries continues to be a bad problem because of tremendous human suffering and the cost of treating it," says study senior author David Marvovitz, M.D., professor of internal medicine at the U-M Medical School.

Although condom use is quite effective, condoms are most successful in preventing infection if used consistently and correctly, which is often not the case.

"That's particularly true in developing countries where women have little control over sexual encounters so development of a long-lasting, self-applied microbicide is very attractive," Markovitz says.

Some of the most promising compounds for inhibiting vaginal and rectal HIV transmission are agents that block HIV prior to integration into its target cell.

The new research describes the complex actions of lectins and their ability to outsmart HIV. Lectins are sugar-binding proteins. They can identify foreign invaders, like a virus, and attach themselves to the pathogen.

The U-M team discovered BanLec, the lectin in bananas, can inhibit HIV infection by binding to the sugar-rich HIV-1 envelope protein, gp120, and blocking its entry to the body.

Co-authors Erwin J. Goldstein, Ph.D., professor emeritus of biological chemistry at U-M and Harry C. Winter, Ph.D., research assistant professor in biological chemistry at U-M, developed the biopurification method to isolate BanLec from bananas. Following their work, the U-M team discovered BanLec is an effective anti-HIV lectin and is similar in potency to T-20 and maraviroc, two anti-HIV drugs currently in clinical use.

Yet therapies using BanLec could be cheaper to create than current anti-retroviral medications which use synthetically produced components, plus BanLec may provide a wider range of protection, researchers say.

"The problem with some HIV drugs is that the virus can mutate and become resistant, but that's much harder to do in the presence of lectins," says lead author Michael D. Swanson, a doctoral student in the graduate program in immunology at the University of Michigan Medical School.

"Lectins can bind to the sugars found on different spots of the HIV-1 envelope, and presumably it will take multiple mutations for the virus to get around them," he says.

Swanson is developing a process to molecularly alter BanLec to enhance its potential clinical utility. Clinical use is considered years away but researchers believe it could be used alone or with other anti-HIV drugs as a vaginal microbicide that prevents HIV infection.

Authors say even modest success could save millions of lives. Other investigators have estimated that 20 percent coverage with a microbicide that is only 60 percent effective against HIV may prevent up to 2.5 million HIV infections in three years.

Authors: Michael D. Swanson, Harry C. Winter, Irwin J. Goldstein and David M. Markovitz, all of U-M.
Reference: The Journal of Biological Chemistry, Vol. 285, Issue 12
Funding: National Institutes of Health, Burroughs Wellcome Fund

Molecular study could push back angiosperm origins

Findings fuel ongoing debates over different approaches to dating the tree of life

Durham, NC – Flowering plants may be considerably older than previously thought, says a new analysis of the plant family tree.

Previous studies suggest that flowering plants, or angiosperms, first arose 140 to 190 million years ago. Now, a paper to be published in the Proceedings of the National Academy of Sciences pushes back the age of angiosperms to 215 million years ago, some 25 to 75 million years earlier than either the fossil record or previous molecular studies suggest.

"If you just looked at the fossil record, you would say that angiosperms originated in the early Cretaceous or late Jurassic," said Michael Donoghue of Yale University. "Most molecular divergence times have shown that they might be older than that," added Yale biologist Jeremy Beaulieu. "But we actually find that they might be Triassic in origin," said Beaulieu. "No one has found a result like that before."

If confirmed, the study could bolster the idea that early angiosperms promoted the rise of certain insects. Modern insects like bees and wasps rely on flowers for nectar and pollen. "The fossil record suggests that a lot of these insect groups originated before angiosperms appeared," said Stephen Smith of the National Evolutionary Synthesis Center. This study shifts the oldest angiosperms back farther in time towards the origin of groups like bees and flies, the scientists say. "If you take our dates and superimpose them on the evolutionary tree for these insect groups, all of a sudden you get a match," said Beaulieu.

To trace the origins of flowering plants, the researchers used genetic comparisons of living plants and clues from fossils to reconstruct the relationships among more than 150 terrestrial plant species. Though their results contradict previous age estimates for angiosperms, they support estimates for other plant groups. "Many of the dates that we get correspond really well to the known fossil record, at least for the origin of land plants and the origin of vascular plants and seed plants," said Donoghue. "But we got a much older date for the origin of angiosperms — one that's really out of whack with the fossil record," Smith added.

This disconnect between molecular and fossil estimates is not unheard of, the authors explained. "We see the same kind of discrepancy in other groups too, like mammals and birds," said Donoghue.

Why the mismatch between different approaches to dating the tree of life?
One possibility, the researchers explained, is that the first flowering plants weren't diverse or abundant enough to leave their mark in the fossil record. "We would expect there to be a time lag between the time of origin and when they became abundant enough to get fossilized," said Smith. "The debate would just be how long."

"Imagine a long fuse burning and then KABOOM! There's a big explosion. Maybe angiosperms were in that fuse state," said Donoghue. "But it's hard to imagine flowering plants would have had a big impact on the origin of major insect groups if that were the case," he added.

Another possibility, the researchers allow, is that the molecular methods may be amiss. "If the angiosperms originated 215 million years ago, then why don't we find them in the fossil record for almost 80 million years?" said Beaulieu. "It could also suggest that our dates are wrong."

"We've done the best analysis we know how to do with the current tools and information," said Donoghue. To improve on previous studies, the researchers used a method that allows for variable rates of evolution across the plant family tree. "Rates of molecular evolution in plants seem to be correlated with changes in life history," he explained. "Older methods assume that rates of molecular evolution don't change too radically from one branch of the evolutionary tree to another. But this newer method can accommodate some fairly major rate shifts." Although researchers have come up with some savvy statistical tricks to account for rate shifts, Donoghue explained, the problem hasn't entirely disappeared.

"As we develop better molecular methods, people would like it if the molecular dates reconciled with the fossil record. Then everybody would be happy," said Donoghue. "But instead the gap is getting wider," he said. "And in the end, that might actually be interesting."

The team's findings will be published early online in the March 15 issue of Proceedings of the National Academy of Sciences.

***CITATION**: Smith, S., J. Beaulieu, and M. Donoghue. (2010). "An uncorrelated relaxed-clock analysis suggests an earlier origin for flowering plants." Proceedings of the National Academy of Sciences doi/10.1073/pnas.1001225107.*

Brain plaques may explain higher risk of Alzheimer's based on mom's history

New imaging tool could eventually lead to earlier detection among pre-symptomatic individuals

NEW YORK A family history of Alzheimer's is one of the biggest risk factors for developing the memory-robbing disease, which affects more than 5 million Americans and is the most common form of senile dementia. Now an international collaboration led by NYU Langone Medical Center researchers has found the likely basis for this heightened familial risk—especially from the maternal side.

Aided by a new version of a brain scanning technique, the researchers discovered a far greater number of protein clumps linked to the disease among healthy adult children of parents with Alzheimer's compared to counterparts with no family history of dementia. The average increase in these clumps, called amyloid-beta plaques, was particularly striking among study volunteers whose mothers had been diagnosed with the disease. The plaques appeared throughout most regions of the brain.

The study examined 42 healthy individuals, including 14 whose mothers had Alzheimer's, 14 whose fathers had Alzheimer's, and 14 counterparts with no family history of the disease. On average, the first group of volunteers showed a 15 percent higher burden of amyloid-beta deposits than those with a paternal family history, and a 20 percent higher burden of the protein clumps than those with no familial risk factors.

The new findings, published in the March 15, 2010, online early edition of Proceedings of the National Academy of Sciences, may help explain why a family history is such a big risk factor for the brain disease - individuals with an affected parent have a four- to ten-fold greater risk than those with no family history.

The study was led by Lisa Mosconi, PhD, research assistant professor of psychiatry at NYU Langone, and colleagues at NYU Langone who collaborated with researchers at the University of Turku in Finland and Weill Cornell Medical Center in New York.

"Given that brain pathology begins to accumulate years ahead of memory problems in Alzheimer's disease, our findings are intriguing," says Dr. Mosconi. "There is a great effort underway to find early markers of disease, before symptoms appear, so that therapeutic approaches will one day delay or ultimately prevent this disease."

Amyloid plaques are one of the hallmarks of Alzheimer's disease, although not everyone with plaques develops the disease. For many years, amyloid-beta plaques could only be measured in autopsied brains, but methods have recently emerged that allow the plaques to be observed in living brains.

The new study combines positron emission tomography (PET) with a fluorescent dye called Pittsburgh Compound B (PiB) that highlights brain amyloid plaques, enabling researchers to actually see the deposits. The dye attaches to plaques and acts like a temporary beacon to highlight their presence during a PET scan. Dr. Mosconi cautions that her team's imaging technique is a potentially powerful research tool and is not ready for use as a diagnostic tool in the clinic.

Plaques begin forming in the brain when, for unknown reasons, normal amyloid-beta proteins change their shape and structure and begin sticking together. The presence of plaques, however, does not necessarily mean an individual will develop Alzheimer's, and much of the harm may arrive well before the plaques appear—no one can yet say whether they are a cause or a consequence of the disease.

It isn't known why the deposits were more common among children of parents with the disease in the study, but Dr. Mosconi suspects that a genetic mechanism is involved. "At this point, we can only speculate that genes that are transmitted from parents, particularly mothers, to their children lead to amyloid depositions, which increase risk for developing dementia," she says.

Dr. Mosconi and her colleagues hope to follow the study's 42 volunteers and more subjects over time to analyze the link between plaque formation and Alzheimer's. For those who never develop dementia, she likewise hopes to determine what preventive factors may be neutralizing the bad effects of amyloid on the brain.

The scanning technique used in the new study also provides more evidence supporting a maternal family link to Alzheimer's, notes Dr. Mosconi, whose previous studies have shown such an association based on reduced glucose metabolism in the brains of healthy adults whose mothers had the disease.

"This imaging study further anchors the risk for Alzheimer's disease associated with having a mother affected by the disease," says Mony J. de Leon, EdD, professor of psychiatry and Director of the Center for Brain Health at NYU Langone Medical Center, and one of the study's authors.

The study's co-authors include Yi Li, Huiyu Wang, John Murray, Schantel Williams, Lidia Glodzik, Wai Tsui and Susan De Santi from NYU Langone Medical Center; Juha Rinne and Noora Scheinin from the University of Turku; Kjell Någren from Turku and Odense University Hospital, Denmark; and Shankar Vallabhajosula from Weill Cornell Medical College.

The study was supported by grants from the National Institutes of Health's National Institute on Aging and National Center for Research Resources, the Alzheimer's Association, the Academy of Finland, the Sigrid Juselius Foundation, and Turku University Hospital.

Nausea Medication Could be a Life-Saver

Dramamine, which is typically used to treat motion sickness, could help patients suffering from heart disease.

By Eric Bland

THE GIST:

**** Anti-nausea drugs could double as heart medication.***

**** Dramamine can slow the heart down, giving medical professionals more time to intervene during a health crisis.***

**** Doctors caution, however, that results are still preliminary.***

Dramamine, the popular anti-nausea medication, also has heart-preserving properties, according to a new study recently published in the journal Nature Biotechnology.

When taken during a heart attack, Dramamine chemically cools the heart, slowing it down to give doctors extra minutes to save a patient's life. The scientists caution the research is still preliminary, and patients with heart diseases should not begin taking daily doses of the drug.

"This study started out as a fishing expedition but has led to some interesting leads," said Paul Brookes, a scientists at University of Rochester and a co-author of the paper describing the results.

According to scientists, Dramamine's effect on the heart is the chemical equivalent of being plunged into ice water. Every year there is a news report of someone falling into an ice covered pond or river. After agonizing minutes without oxygen the person is pulled out of the water, warmed up and somehow survives.

Usually only a few minutes without oxygen causes death. The icy water slows down the body's metabolism, extending the amount of time doctors, nurses or paramedics can successfully save a patient.

The study doesn't mean patients with heart disease should start taking Dramamine, says Brookes. The study was done in mice and rats, not humans. Scientists also don't know the exact cellular or molecular mechanisms Dramamine induces to protect the heart.

Dramamine also has well known side effects, including drowsiness and even hallucinations at high doses. Added together, human trials of Dramamine's heart protective effects are years away, said Brookes.

Dramamine wasn't the only drug the scientists identified. The scientists screened more than 3,700 different drugs to find new candidates to help patients survive a heart attack.

Of the more than 3,700 drugs, about 250 were identified as potentially helpful for hearts. Dramamine was one of the 140 drugs already known to doctors, many of which are approved heart medication. That leaves 110 other drugs that could help patients at risk for heart attacks that need to be explored, said Brookes.

The drug screening method is "pretty exciting," said James Downey, a doctor at the University of Alabama, Mobile. The technique will give scientists a new way to identify potentially life-saving drugs for any number of diseases or conditions. Downey, however, agrees with Brookes that any treatment using Dramamine is still years - and many a clinical trial – away.

New research shows babies are born to dance

Researchers have discovered that infants respond to the rhythm and tempo of music and find it more engaging than speech. The findings, based on the study of infants aged between five months and two years old, suggest that babies may be born with a predisposition to move rhythmically in response to music.

The research was conducted by Dr Marcel Zentner, from the University of York's Department of Psychology, and Dr Tuomas Eerola, from the Finnish Centre of Excellence in Interdisciplinary Music Research at the University of Jyvaskyla.

Dr Zentner said: "Our research suggests that it is the beat rather than other features of the music, such as the melody, that produces the response in infants. "We also found that the better the children were able to synchronize their movements with the music the more they smiled.

"It remains to be understood why humans have developed this particular predisposition. One possibility is that it was a target of natural selection for music or that it has evolved for some other function that just happens to be relevant for music processing."

Infants listened to a variety of audio stimuli including classical music, rhythmic beats and speech. Their spontaneous movements were recorded by video and 3D motion-capture technology and compared across the different stimuli. Professional ballet dancers were also used to analyse the extent to which the babies matched their movement to the music.

The findings are published today in the journal Proceedings of the National Academy of Sciences Online Early Edition. *The research was part-funded by a grant from the Swiss National Science Foundation.*

Notes to editors: The research "Rhythmic engagement with music in infancy" will be available in full at www.pnas.org.

Hazards: Report Finds High Rate of Herpes in U.S.

By RONI CARYN RABIN

One in six Americans aged 14 to 49 are infected with genital herpes, making the virus - herpes simplex 2 - one of the most common sexually transmitted diseases in the United States, according to a new report from the Centers for Disease Control and Prevention.

Although infection rates have not increased in recent years, health officials are concerned because individuals infected with genital herpes are at greater risk for infection with the virus that causes AIDS and for transmitting it to others.

Research shows that people with genital herpes are two to three times as likely to acquire H.I.V. as those without herpes, said Dr. John M. Douglas Jr., director of the agency's division for preventing sexually transmitted diseases. "And herpes can also make H.I.V.-infected individuals more likely to transmit H.I.V. to others," he added.

The latest figures, derived from the C.D.C.'s National Health and Nutrition Examination Survey for 2005-8, found striking disparities in infection rates, with women infected at almost twice the rate of men, and blacks three times as likely to be infected as whites. Black women have the highest rates of infection, with almost half infected. Biological factors and community trends are most likely responsible for the disparate infection rates, officials said.

Studies provide more support for health benefits of coffee

Multitudes of people worldwide begin each day with a cup of steaming hot coffee. Although it is sometimes referred to as "the devil's brew," coffee contains several nutrients (eg, calcium) as well as hundreds of potentially biologically active compounds (eg, polyphenols) that may promote health. For instance, observational studies have suggested a beneficial link between coffee consumption and type 2 diabetes. Determining whether or not this association is causative, however, requires controlled intervention trials. Two articles published in the April 2010 issue of The American Journal of Clinical Nutrition report results of 2 studies conducted to lend additional information concerning the potential health benefits of coffee. These studies provide additional support for the emerging health benefits of coffee. Rigorous clinical intervention trials will be needed to understand more fully the biological mechanisms.

The studies by Kempf and Sartorelli "add to a growing literature suggesting that my steaming cup of morning coffee might help me stay healthy," said ASN Spokesperson Shelley McGuire, PhD. "I'm a research scientist, but I still trust that foods and beverages which have been part of our culture for generations are probably good for us, or at least they're probably not bad for us in moderation! Of particular interest is the well-controlled clinical trial that suggests coffee can lower chronic inflammation and even raise our 'good' cholesterol. I for one will enjoy my coffee even more in the weeks to come." *Access the full text of the studies here:*
http://asn-cdn- remembers.s3.amazonaws.com/8f0710073b3ca5a420c3d6d612c5d73d.pdf
http://asn-cdn-remembers.s3.amazonaws.com/2ee7a9f54ae5943202374d5d3c71d63f.pdf

Drug Helps Diabetics, Trial Finds

By RONI CARYN RABIN

An inexpensive, generic anti-inflammatory drug from the aspirin family helped patients in a clinical trial manage their Type 2 diabetes and lower their blood sugar, adding to evidence that inflammation plays a role in diabetes, and possibly pointing to new therapeutic approaches to the disease.

The drug, salsalate, which is related to aspirin but is not as hard on the stomach, has been used for years to treat arthritis and joint pain. Patients who took it as part of a randomized clinical trial led by researchers at the Joslin Diabetes Center improved their blood sugar levels after three months, with those taking the highest dose lowering their hemoglobin A1C scores by 0.5 percent on average. Patients who took the drug also lowered their triglycerides.

"The potential is really exciting," said Dr. Allison B. Goldfine, Joslin's director of clinical research and the lead author of the paper, which will be published in Tuesday's Annals of Internal Medicine. "We may have a new class of therapeutic agents to treat patients with Type 2 diabetes, and when you have a new safe, effective and inexpensive agent, that's pretty exciting."

Even more importantly, the work may help unravel the root causes of diabetes, said Dr. Steven E. Shoelson, the paper's senior author and head of Joslin's research section on pathophysiology and molecular pharmacology, and professor of medicine at Harvard Medical School. "If we can figure out how this is working, we can figure out some of the root causes of diabetes and how obesity promotes inflammation, and how inflammation promotes diabetes and other chronic health problems," Dr. Shoelson said.

Both authors injected a note of caution, however, saying more research was needed before doctors start prescribing salsalate.

Just over 100 patients completed the randomized clinical trial and some experienced negative side effects, like an increase in LDL, or so-called bad cholesterol.

The most common side effect was experienced by patients who were on diabetes medications called sulfonylureas and experienced episodes of mild hypoglycemia, a drop in blood sugar that can be dangerous.

Experts who were not involved in the multi-center trial agreed larger trials were needed, and said the impact of the drug on blood glucose levels was moderate. But they said the findings were exciting because they suggested Type 2 diabetes could be treated by targeting the underlying inflammation.

"It expands the therapeutic weaponry against the disease," said Dr. Domenico Accili, director of the Columbia University Diabetes and Endocrinology Research Center.

Since atherosclerosis is also considered an inflammatory state, this approach may also potentially reduce the risk of cardiovascular complications associated with diabetes, he said.

Dr. Meredith Hawkins, a professor of medicine at Albert Einstein, also said the work showed that "inflammation is a good target in terms of treating diabetes - and that's something that we've been talking about for a long time."

The research is being supported by the National Institutes of Health and the National Institute of Diabetes and Digestive and Kidney Diseases.

Salsalate sells for less than a quarter a pill, and does not present the opportunity for profit that would attract large pharmaceutical companies to do the research. But with an estimated 23.6 million Americans already suffering from diabetes and an additional 57 million having pre-diabetes, the federal government has a huge interest in developing new treatments.

As part of the trial, researchers at 17 different clinical centers randomly assigned 108 individuals ages 18 to 75 to four different treatment regimens, three of which included different amounts of salsalate in three daily doses while patients in the fourth group were given placebos, or dummy pills.

The patients continued with their regular Type 2 diabetes treatment regimen throughout the study. After three months, patients who were taking salsalates were far more likely to have improved their blood sugar levels than those on placebo, with patients on the highest doses of 4 grams a day having the most improvement.

A Host of Mummies, a Forest of Secrets

By NICHOLAS WADE

In the middle of a terrifying desert north of Tibet, Chinese archaeologists have excavated an extraordinary cemetery. Its inhabitants died almost 4,000 years ago, yet their bodies have been well preserved by the dry air.

The cemetery lies in what is now China's northwest autonomous region of Xinjiang, yet the people have European features, with brown hair and long noses. Their remains, though lying in one of the world's largest deserts, are buried in upside-down boats. And where tombstones might stand, declaring pious hope for some god's mercy in the afterlife, their cemetery sports instead a vigorous forest of phallic symbols, signaling an intense interest in the pleasures or utility of procreation.

***SYMBOLISM** Archaeologists believe the hundreds of 13-foot poles at the Small River Cemetery in a desert in Xinjiang Province, China, were mostly phallic symbols.* **Liu Yu Sheng**

The long-vanished people have no name, because their origin and identity are still unknown. But many clues are now emerging about their ancestry, their way of life and even the language they spoke.

Their graveyard, known as Small River Cemetery No. 5, lies near a dried-up riverbed in the Tarim Basin, a region encircled by forbidding mountain ranges. Most of the basin is occupied by the Taklimakan Desert, a wilderness so inhospitable that later travelers along the Silk Road would edge along its northern or southern borders.

In modern times the region has been occupied by Turkish-speaking Uighurs, joined in the last 50 years by Han settlers from China. Ethnic tensions have recently arisen between the two groups, with riots in Urumqi, the capital of Xinjiang. A large number of ancient mummies, really desiccated corpses, have emerged from the sands, only to become pawns between the Uighurs and the Han.

The 200 or so mummies have a distinctively Western appearance, and the Uighurs, even though they did not arrive in the region until the 10th century, have cited them to claim that the autonomous region was always theirs. Some of the mummies, including a well-preserved woman known as the Beauty of Loulan, were analyzed by Li Jin, a well-known geneticist at Fudan University, who said in 2007 that their DNA contained markers indicating an East Asian and even South Asian origin.

The mummies in the Small River Cemetery are, so far, the oldest discovered in the Tarim Basin. Carbon tests done at Beijing University show that the oldest part dates to 3,980 years ago. A team of Chinese geneticists has analyzed the mummies' DNA.

Despite the political tensions over the mummies' origin, the Chinese said in a report published last month in the journal BMC Biology that the people were of mixed ancestry, having both European and some Siberian genetic markers, and probably came from outside China. The team was led by Hui Zhou of Jilin University in Changchun, with Dr. Jin as a co-author.

All the men who were analyzed had a Y chromosome that is now mostly found in Eastern Europe, Central Asia and Siberia, but rarely in China. The mitochondrial DNA, which passes down the female line, consisted of a lineage from Siberia and two that are common in Europe. Since both the Y chromosome and the mitochondrial DNA lineages are ancient, Dr. Zhou and his team conclude the European and Siberian populations probably intermarried before entering the Tarim Basin some 4,000 years ago.

The Small River Cemetery was rediscovered in 1934 by the Swedish archaeologist Folke Bergman and then forgotten for 66 years until relocated through GPS navigation by a Chinese expedition. Archaeologists began excavating it from 2003 to 2005. Their reports have been translated and summarized by Victor H. Mair, a professor of Chinese at the University of Pennsylvania and an expert in the prehistory of the Tarim Basin.

As the Chinese archaeologists dug through the five layers of burials, Dr. Mair recounted, they came across almost 200 poles, each 13 feet tall. Many had flat blades, painted black and red, like the oars from some great galley that had foundered beneath the waves of sand.

At the foot of each pole there were indeed boats, laid upside down and covered with cowhide. The bodies inside the boats were still wearing the clothes they had been buried in. They had felt caps with feathers tucked in the brim, uncannily resembling Tyrolean mountain hats. They wore large woolen capes with tassels and leather boots. A Bronze Age salesclerk from Victoria's Secret seems to have supplied the clothes beneath — barely adequate woolen loin cloths for the men, and skirts made of string strands for the women.

Within each boat coffin were grave goods, including beautifully woven grass baskets, skillfully carved masks and bundles of ephedra, an herb that may have been used in rituals or as a medicine.

In the women's coffins, the Chinese archaeologists encountered one or more life-size wooden phalluses laid on the body or by its side. Looking again at the shaping of the 13-foot poles that rise from the prow of each woman's boat, the archaeologists concluded that the poles were in fact gigantic phallic symbols.

The men's boats, on the other hand, all lay beneath the poles with bladelike tops. These were not the oars they had seemed at first sight, the Chinese archaeologists concluded, but rather symbolic vulvas that matched the opposite sex symbols above the women's boats. "The whole of the cemetery was blanketed with blatant sexual symbolism," Dr. Mair wrote. In his view, the "obsession with procreation" reflected the importance the community attached to fertility.

Arthur Wolf, an anthropologist at Stanford University and an expert on fertility in East Asia, said that the poles perhaps mark social status, a common theme of tombs and grave goods. "It seems that what most people want to take with them is their status, if it is anything to brag about," he said.

Dr. Mair said the Chinese archaeologists' interpretation of the poles as phallic symbols was "a believable analysis." The buried people's evident veneration of procreation could mean they were interested in both the pleasure of sex and its utility, given that it is difficult to separate the two. But they seem to have had particular respect for fertility, Dr. Mair said, because several women were buried in double-layered coffins with special grave goods.

Living in harsh surroundings, "infant mortality must have been high, so the need for procreation, particularly in light of their isolated situation, would have been great," Dr. Mair said. Another possible risk to fertility could have arisen if the population had become in-bred. "Those women who were able to produce and rear children to adulthood would have been particularly revered," Dr. Mair said.

Several items in the Small River Cemetery burials resemble artifacts or customs familiar in Europe, Dr. Mair noted. Boat burials were common among the Vikings. String skirts and phallic symbols have been found in

Bronze Age burials of Northern Europe. There are no known settlements near the cemetery, so the people probably lived elsewhere and reached the cemetery by boat. No woodworking tools have been found at the site, supporting the idea that the poles were carved off site.

The Tarim Basin was already quite dry when the Small River people entered it 4,000 years ago. They probably lived at the edge of survival until the lakes and rivers on which they depended finally dried up around A.D. 400. Burials with felt hats and woven baskets were common in the region until some 2,000 years ago.

The language spoken by the people of the Small River Cemetery is unknown, but Dr. Mair believes it could have been Tokharian, an ancient member of the Indo-European family of languages. Manuscripts written in Tokharian have been discovered in the Tarim Basin, where the language was spoken from about A.D. 500 to 900. Despite its presence in the east, Tokharian seems more closely related to the "centum" languages of Europe than to the "satem" languages of India and Iran. The division is based on the words for hundred in Latin (centum) and in Sanskrit (satam).

The Small River Cemetery people lived more than 2,000 years before the earliest evidence for Tokharian, but there is "a clear continuity of culture," Dr. Mair said, in the form of people being buried with felt hats, a tradition that continued until the first few centuries A.D.

An exhibition of the Tarim Basin mummies opens March 27 at the Bowers Museum in Santa Ana, Calif. — the first time that the mummies will be seen outside Asia.

An earlier version of this article incorrectly described Xinjiang as a province rather than an autonomous region.

SBRT eliminates tumors with promising survival for early stage inoperable lung cancer patients

Philadelphia – Highly-focused stereotactic body radiation therapy (SBRT) can eliminate the targeted tumor while avoiding treatment-related illness and may ultimately improve survival for patients with inoperable non-small cell lung cancer, according to early findings of a Radiation Therapy Oncology Group study published in the March 17 cancer-themed issue of the Journal of the American Medical Association. Stereotactic body radiation therapy (SBRT) is a noninvasive cancer treatment in which numerous small, highly focused, and accurate radiation beams are used to deliver potent doses in 1 to 5 treatments to tumor targets.

"The primary finding and perhaps most exciting aspect to this prospective study was the high rate of primary tumor control (97.6 percent at 3 years). Primary tumor control is an essential requirement for the cure of lung cancer. Stereotactic body radiation therapy as delivered in RTOG 0236 provided more than double the rate of primary tumor control previous reported for conventional radiotherapy suggesting that this technique could provide a significant step forward in the battle against this type of lung cancer," said Robert Timmerman, MD, of the University of Texas Southwestern Medical Center, Dallas, principal investigator on the RTOG study.

Currently, patients with inoperable early stage lung cancer are generally offered conventional radiation treatment (most commonly given during 20-30 outpatient treatments) or observed without specific cancer therapy. However, study authors indicate that neither of these approaches achieves ideal outcomes.

"Conventional radiotherapy fails to provide long-term control of the primary lung tumor in approximately two-thirds (60 percent to 70 percent) of patients. Most ultimately die specifically from progressive lung cancer with observation, and 2-year survival is less than 40 percent with either approach. Our study suggests that stereotactic body radiation therapy is a new option that produces better outcomes and may represent an updated, and ultimately more successful, approach to the treatment of patients with early stage inoperable lung cancer," said Timmerman.

This is the first North American multicenter, cooperative group study to test SBRT in treating medically inoperable patients with early stage non-small cell lung cancer. Dr. Timmerman and RTOG member investigators enrolled 59 patients to this phase II study that included patients 18 years or older with biopsy-proven peripheral T1-T2N0M0 non-small cell tumors (measuring less than 5 cm. in diameter) and medical conditions that would not allow surgical treatment. Radiation treatment lasted between 1.5 and 2 weeks. The study opened May 2004 and closed October 2006, with data analyzed through August 2009. The final study population included 55 evaluable patients (44 with T1 tumors and 11 patients with T2 tumors), with a median (midpoint) follow-up of 33.4 months.

The primary outcome measured for the study was 2-year actuarial primary tumor control; secondary end points were disease-free survival (i.e., primary tumor, involved lobe, regional, and disseminated recurrence [the reappearance or return of a cancer in multiple areas of the body]), treatment-related toxicity, and overall survival.

Of all the patients in the study, only one experienced a documented tumor recurrence or progression at the primary site. The 3-year primary tumor control rate was 97.6 percent. Three patients had recurrence within the involved lobe; the 3-year primary tumor and involved lobe (local) control rate was 90.6 percent. Combining

local and regional failures, the 3-year local-regional control rate was 87.2 percent. Disseminated recurrence as some component of recurrence was reported in 11 patients. The 3-year rate of disseminated failure was 22.1 percent with 8 such failures occurring prior to 24 months.

Disease-free survival and overall survival at 3 years were 48.3 percent and 55.8 percent, respectively. Median disease-free survival and overall survival for all patients were 34.4 months and 48.1 months, respectively. Seven patients (12.7 percent) and two patients (3.6 percent) were reported to experience protocol-specified treatment-related grade 3 and 4 adverse events, respectively. No grade 5 treatment-related adverse events were reported. Higher grades indicate greater severity of adverse event, with grade 5 indicating death.

"While this is a phase II study involving a relatively small patient sample, these results suggest that this technique could greatly improve survival rates for patients with inoperable non-small cell lung cancer. For this group of patients there simply has not been significant advance in survival rates in some time. These results certainly dictate that further study of SBRT is warranted. We are optimistic that the technique holds promise for these patients," said Timmerman

According to Walter J. Curran, Jr., MD, the RTOG Group Chair, and the Executive Director of the Winship Cancer Institute of Emory University, "RTOG 0236 demonstrated that technologically intensive treatments like SBRT can be performed in the cooperative group setting so long as effective quality control measures are in place to assure patient safety. As the preeminent group conducting multi-institutional clinical trials of novel radiation therapy techniques, RTOG is building on these results to improve patient outcomes and quality of life with trials designed to address the rather high rate of disseminated failure observed after treatment, determine a safe and effective dose for central lung tumors, and refine the dose of SBRT for peripheral tumors."

RTOG is a National Cancer Institute-funded national clinical trials group and is administered by the American College of Radiology. JAMA. 2010;303[11]:1070-1076.

Cloves are the best natural antioxidant

Using spices eaten in the Mediterranean diet as natural antioxidants is a good way forward for the food industry, given the beneficial health effects of these products. This has been shown by researchers from the Miguel Hernández University (UMH), who have put the clove in first place.

Researchers from the Miguel Hernández University have identified cloves (Syzygium aromaticum) as the best antioxidant spice, due to the fact they contain high levels of phenolic compounds, as well as having other properties.

"Out of the five antioxidant properties tested, cloves had the highest capacity to give off hydrogen, reduced lipid peroxidation well, and was the best iron reducer", Juana Fernández-López, one of the authors of the study and a researcher at the UMH, tells SINC.

As a result, the research study published in the latest issue of the Flavour and Fragrance Journal ranks this spice as the best natural antioxidant.

"The results show that use of the natural oxidants occurring in spices used in the Mediterranean diet, or their extracts, is a viable option for the food industry, as long as the organoleptic characteristics of the food product are not affected", adds the researcher.

"These substances exhibit high antioxidant capacity, and could have beneficial effects for health", says the researcher

The team also evaluated the antioxidant effect of the essential oils from other spices used in the Mediterranean diet – oregano (Origanum vulgare), thyme (Thymus vulgaris), rosemary, (Rosmarinus funcionarios cinalis) and sage (Salvia funcionarios cinalis).

The objective of the study is to enable these spices to be incorporated into food products (above all meat products) as natural antioxidants.

Changing the food industry

"Lipid oxidation is one of the main reasons for foods deteriorating, and causes a significant reduction in their nutritional value, as well as loss of taste", says Fernández-López.

These alterations lead to a reduction in the useful lifespan of the food product. To avoid such deterioration, the food industry uses synthetic antioxidants in its products. However, as these are chemical compounds, questions have been raised about their potential toxicity and side-effects.

As a result, there is a growing interest in using plant-based products (spices, aromatic and medicinal plants) with potential antioxidant activity, in order to replace the synthetic antioxidants with "natural" substances.

***References**: Manuel Viuda-Martos, Yolanda Ruiz Navajas, Elena Sánchez Zapata, Juana Fernández-López y José A. Pérez-Álvarez. "Antioxidant activity of essential oils of five spice plants widely used in a Mediterranean diet". Flavour and Fragrance Journal 25, 13-19, enero - febrero de 2010.*

Earth's forgotten youth - and beyond

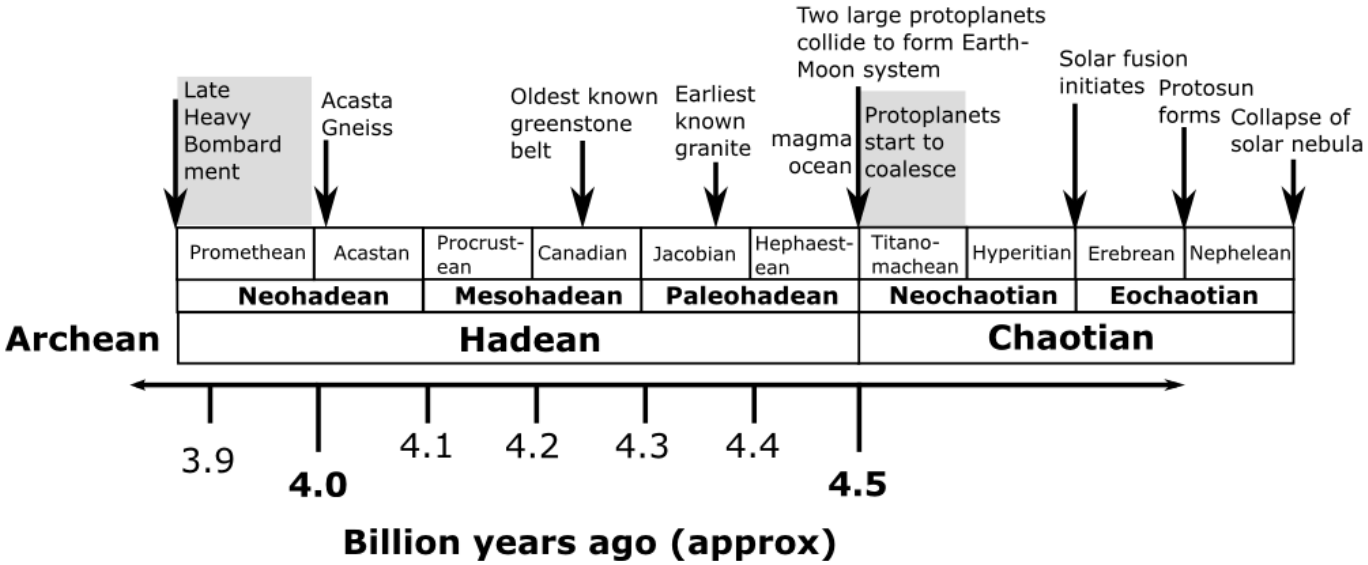
A post by Chris RowanResearchBlogging.org

The further back in time we go, the more and more fragmented the Earth's geological record becomes. Whilst not exactly common, rocks with ages up to about 3.5 billion years old are found at multiple points on the Earth's surface. However, rocks older than this are much less common. Extensive outcrops older than about 3.8 billion years are exceptionally rare, possibly because a series of very large meteorite impacts prior to this time - the Late Heavy Bombardment - largely destroyed any older bits of crust. The Acasta Gneiss in northern Canada, dated at around 4.03 billion (4030 million) years, is generally regarded as the oldest known outcrop of crust, although a recent study has claimed that the Nuvvuagittuq greenstone belt, also in northern Canada, may be as old as 4280 million years. The only known bits of the Earth that are older are 4.2-4.4 billion year-old zircon crystals found in the Jack Hills Conglomerate in Australia; the conglomerate itself was deposited about 3 billion years ago, but it contains debris eroded from much older, and now long-vanished, bits of crust.

Two or three data points is not a hell of a lot to go on when trying to reconstruct the evolution of the early Earth, especially when the material involved is far from pristine (the Acasta Gneiss, being a gneiss. has been partially remelted, for example). It is therefore no surprise that the geological timescale for the period between the Earth's formation, about 4.56 billion years ago, and the start of the Archean Eon, usually pegged at about 3.8 billion years ago, is rather lacking in detail. This period is usually referred to as the 'Hadean', which is more of a reference to the presumed conditions on the Earth's surface than a subtle pointer to the fact that we don't know what the hell was really going on.

However, this has not stopped Colin Goldblatt and his co-authors having a go at adding a bit more structure to the Earth's earliest days - and beyond. The 'Chaotian' eon at the start of their proposed new timescale is a common framework for the entire solar system, beginning with the gravitational collapse of the gas cloud that it would eventually form from. Key events - such as the initiation of solar fusion, or the first interactions between sizeable protoplanets that condensed from the protoplanetary disk - mark the boundaries between different eras and periods within the Chaotian. The start of the Hadean is marked by the collision of the proto-Earth, which the authors call Tellus, with another Mars-sized protoplanet, forming the Earth-Moon system.

Thus, the Chaotian marks the time when solar system first became a distinct entity from the galactic neighbourhood; the beginning of the Hadean is when the Earth's geological history begins to be shaped as much by internal processes, such as mantle convection, as by external events such as collisions with other protoplanets, Similarly, from beginning of the Archean, at the end of the Late Heavy Bombardment, internal processes start to completely dominate the Earth's geological evolution; extraterrestrial collisions can still have significant geochemical and biological impacts, but they no longer melt the entire crust. Conceptually, I find this quite a nice way of looking at it.



Proposed new timescale for the formation of the solar system (Chaotian) and the evolution of the early Earth (Hadean).

The authors also attempt to subdivide the Hadean, but because we still don't understand the key events in the Earth's geological events over this period, it's not quite as successful. The Hephaestean period probably covers the recovery from the Moon-forming impact. The Jacobian, Canadian and Acastan periods refer to the Jack Hills zircons, Nuvvuagittuq greenstone belt and Acasta Gneiss, respectively, but although these outcrops can give us clues about what the Earth was like when they first formed, it is a bit risky to try to characterise an

entire planetary system from one sampling point. For example, the Jack Hills zircons tell us that granite - in other words, continental crust - was forming 4.4 billion years ago, but this is only a minimum age; we have no evidence that it wasn't forming before that. Also, for all we know greenstone belts were also forming at exactly the same time, and have just not been preserved. The small amount of data we have available means that a single new outcrop might force the entire timescale to be redrafted.

It's difficult to know if we're ever going to be able to construct a truly robust, process based timescale for the first 700 million years of Earth's history, because it's unclear how much we'll ever truly know about the Hadean. Still, this is an interesting attempt to set the story of our planet's birth into a slightly more structured framework.

Goldblatt, C., Zahnle, K. J., Sleep, N. H., & Nisbet, E. G (2010). The Eons of Chaos and Hades Solid Earth, 1, 1-3

Crystals + sound + water = clean hydrogen fuel

* 12:41 16 March 2010 **by Phil McKenna**

Every drop of water is stuffed with the greenest of fuels, hydrogen, but getting it out is a challenge. A new material raises the prospect of doing so using noise pollution – from major roads, for example.

A team at the University of Wisconsin-Madison made crystals of zinc oxide that, when immersed in water, absorb vibrations and develop areas of strong negative and positive charge. These charges rip apart nearby water molecules, releasing hydrogen and oxygen gas.

"This is like a free lunch," says lead researcher Huifang Xu. "You are getting energy from the environment just like solar cells capture energy from the sun."

Underwater operator

Xu and colleagues generate hydrogen using a new variation on piezoelectric crystals – materials that generate a voltage when strained and which are being investigated as a way to generate electricity from movement.

The new crystals, however, are designed to be submerged, so the charge they generate instead pulls apart water molecules to release hydrogen and oxygen gas, a mechanism Xu's team calls the piezoelectrochemical effect.

Xu and colleagues grew thin microfibers of highly flexible zinc oxide crystals that flex when subjected to vibration, for example due to sound waves. They showed that ultrasonic vibrations under water cause the fibres to bend between 5 and 10 degrees at each end, creating an electrical field with a high enough voltage to split water and release oxygen and hydrogen.

Growing fibres with different dimensions changes the type of vibration they absorb best. For instance, it should be possible to tune them to maximise energy production from the vibrations caused by water flowing past or any other sound, say Xu.

Efficiency issue

Xu says that lab tests suggested the material can convert 18 per cent of the energy it absorbs from vibration into energy locked up in hydrogen gas, which can be released by burning.

Conventional piezoelectric materials are not as efficient at converting vibrations into electricity, and typically achieve around a 10 percent conversion rate. Using the charge a material generates indirectly, to split water, instead of directly to drive current, accounts for the difference, says Xu. The new materials could be used to develop systems that generate hydrogen from the noise of anything from machinery to crashing waves, he adds.

"It's a good idea," says Jinhui Song of Georgia Tech University, Atlanta. Because there is no need to create a circuit, devices based on the new crystals could be simpler than those based on conventional dry piezoelectrics, he points out. "They can reduce the complexity of the device."

However, he's sceptical that the wet devices should necessarily be more efficient. In principle, says Song, the energy generated by a material should be the same however it is deployed.

Journal reference: Journal of Physical Chemistry Letters (DOI: 10.1021/jz100027t

As Girth Grows, Risk of Sudden Cardiac Death Shrinks

Study Reaffirms "Obesity Paradox": Obese patients at lower risk of sudden cardiac death compared to non-obese patients

Obesity has long been identified as a risk factor for cardiovascular disease and heart failure. But, a new study conducted by researchers at the University of Rochester Medical Center found that being skinny confers no advantage when it comes to the risk of dying suddenly from cardiac causes.

Scientists found that non-obese heart failure patients – including overweight, normal and underweight patients – had a 76 percent increase in risk of sudden cardiac death compared to obese heart failure patients. Normal and underweight patients showed a startling 99 percent increase in risk for sudden cardiac death compared to obese patients.

The results were presented today at the American College of Cardiology Annual Scientific Session in Atlanta. The study, by researchers from one of the world's leading groups on sudden cardiac death, is the first to assess the relation between BMI and the risk of sudden cardiac death.

"This study is important because it not only answers questions regarding the risk of sudden cardiac death in different types of heart failure patients, but poses several new questions that need to be explored," said corresponding study author Ilan Goldenberg, M.D., research associate professor of Medicine in the Cardiology Division. "Why do obese heart failure patients see a risk advantage? Why do normal weight patients have a significantly different risk profile than those who are slightly overweight? These are important questions that may have treatment implications in the future."

The researchers at the University's Heart Research Follow-Up Program examined the risk of sudden cardiac death in 1,231 patients who had suffered at least one prior heart attack and had been diagnosed with a low ejection fraction, a measurement of how much blood is pumped from the heart with each beat. Their analysis found that decreased BMI or body mass index was associated with a large increase in the risk of sudden cardiac death. These findings highlight the "obesity paradox," a phenomenon long recognized by cardiologists that, once afflicted, obese heart failure patients fare better than their slimmer counterparts. This study adds to a growing body of conflicting data regarding the relation of BMI to outcome in patients with heart failure.

"When we started this study we were hoping the data would disprove the obesity paradox," said Bonnie Choy, co-lead author and a second year medical student at the University's School of Medicine and Dentistry. "Our study is the first to create and analyze subcategories within non-obese patients, looking at overweight, normal and underweight patients, but even with this advanced analysis we still the saw an inverse relationship between BMI and sudden cardiac death."

The science behind the obesity paradox in the heart failure population is unresolved, but some researchers believe timing may have something to do with it. One possible explanation is that the long-term negative effects of conventional risk factors, such as increased BMI, may be overwhelmed by the short-term effects of other factors on heart failure mortality. In addition, survival advantages that exist in obese patients with heart failure may, in the short term, outweigh the harmful effects of increased BMI.

"Obese patients are hard on their bodies; many don't eat right, don't exercise, and many smoke," explained Eric Hansen, co-lead author and also a second year medical student at the University of Rochester. "If their bodies are surviving this bad treatment then perhaps they are better equipped, from a genetic standpoint, to live with heart failure."

Compared to the overweight, normal and underweight patients, obese patients were younger, had a higher ejection fraction, higher blood pressure, diabetes and were more likely to be smokers. BMI was calculated as weight in kilograms divided by the square of height in meters for all study participants. The clinical definition of obesity – BMI ≥30 kg/m2 – was used. Overweight patients fell into the 25 to 29 kg/m2 range of BMI values and normal/underweight patients fell into the <25 kg/m2 range of values.

In addition to evaluating the relationship between BMI and sudden cardiac death, researchers assessed the effect of BMI on the benefit of implantable cardioverter defibrillator (ICD) therapy. An implantable cardioverter defibrillator is a medical device about the size of a pager that is surgically implanted in the chest under local anesthesia. The device detects irregular and potentially fatal heart rhythms (arrhythmias), which often lead to sudden cardiac death, and shocks the heart back into a normal rhythm. Researchers found that implantable cardioverter defibrillator therapy was more effective in the non-obese patients with lower BMI values who were at higher risk for sudden cardiac death. These findings may help identify patients who would get the most benefit from an ICD – patients with a lower BMI.

Sudden cardiac death claims up to 330,000 American lives every year, accounting for about half of all cardiac deaths. Sudden cardiac arrest, a condition in which the heart suddenly and unexpectedly stops beating, leads to sudden cardiac death if it is not treated within minutes. Most cases of sudden cardiac arrest are due to abnormal heart rhythms that can result from blockage of coronary arteries or scarring from a prior heart attack. Certain drugs can also trigger abnormal rhythms and death.

In addition to Goldenberg, Choy and Hansen worked closely with Cardiology faculty members Arthur J. Moss, M.D., and Wojciech Zareba, M.D., Ph.D., to complete this study.

Hobbit Ancestors Once Colonized Indonesia Island

Reuters

HONG KONG Ancestors of a hobbit-like species of humans may have colonized the Indonesian island of Flores as far back as a million years ago, much earlier than thought, according to a new study published Thursday.

These early ancestors, or hominins, were previously thought to have arrived on the island about 800,000 years ago but artifacts found in a new archaeological site suggest they might have been around even earlier.

In a paper published in Nature, researchers said their findings suggest these hominins may have evolved into tiny hobbit-like humans, or "Flores man," who stood about a meter tall and had skulls the size of grapefruit.

Skeletal remains of an 18,000-year-old "Flores man" were discovered about five years ago and scientists then determined it belonged to a species of human completely new to science. Named Homo floresiensis, after the island on which it was found, the tiny human has also been dubbed "hobbit," after the tiny creatures from the "Lord of the Rings."The arrival of hominins is also believed to have resulted quickly in the mass death of giant tortoises and the Stegondon sondaari, a pygmy elephant, on the island.

In their paper, the researchers said they found 45 stone tools in Wolo Sege in the Soa basin in Flores. Led by Adam Brumm at the Center of Archaeological Science in the University of Wollongong in New South Wales, Australia, the researchers used new dating methods and found that the stone tools were about a million years old.

"It is now clear, however, in light of the evidence from Wolo Sege, that hominins were present on Flores (a million years ago). This suggests that the non-selective, mass death of Stegondon sondaari and giant tortoise ... could represent a localized or regional extinction," they wrote in their paper.

"Flores man" is thought to be a descendant of homo erectus, who had a large brain, was full-sized and spread out from Africa to Asia about two million years ago.

Scientists suspect "Flores man" lived at the same time as modern humans and became extinct after a massive volcanic eruption on the island around 12,000 years ago. *(Reporting by Tan Ee Lyn; Editing by Sugita Katyal)*

Algae's solar electrons hijacked to steal power

* 10:18 17 March 2010 **by Colin Barras**

An international gang of biologists has carried out an audacious heist, stealing valuable electrons from photosynthesising algae.

The power grab could open a route to more efficient exploitation of photosynthesis to power machines: with biofuels we are already converting solar power into a form that engines can use, but almost three-quarters of the sunlight energy absorbed by the organisms is lost before it can be turned into the sugars or starches used to make biofuels.

Grabbing photosynthetic energy earlier in the process should allow much more to be extracted, says WonHyoung Ryu at Yonsei University in Seoul, South Korea. "Theoretically we should be able to collect all photosynthetic electrons."

Trapped cells

Ryu worked with colleagues at Stanford University, California, to plug gold electrodes directly into algal cells and draw off electrons carrying energy absorbed from light.

The team captured the unicellular algae Chlamydomonas in tiny traps. They attached an ultra-sharp gold electrode to an atomic force microscope and inserted its 30-nanometre-wide tip into the photosynthesising organs – chloroplasts – of an algal cell. That electrode was connected to an electric current meter, and a second gold electrode was placed in the cell's growth medium to complete the circuit.

The light reaching an alga's chloroplasts is used by proteins inside to split oxygen from water, releasing electrons that are passed between other molecules to provide energy to drive chemical reactions.

When Ryu and colleagues shone a halogen lamp on their alga, those electrons were siphoned off by the electrode instead. Their circuit registered a current of 1.2 picoamps – which is equivalent to a yield of 0.6 milliamps per square centimetre. By increasing the light intensity that value rises to a maximum of 6 milliamps per square centimetre, Ryu says.

By contrast, some silicon solar cells have a current density of 35 milliamps per square centimetre. Despite that, Ryu thinks his algae could still find a job in power generation. "The solar cell efficiency is also related to the wavelength of light," he says. "We believe our bio-solar system may provide higher efficiency than the silicon-based solar cells at particular wavelengths." Chlorophyll, for instance, has evolved to absorb blue and red light well, but doesn't absorb much green light, hence its colour.

Where next?

The team thinks the gold electrode managed to snaffle around 20 per cent of the total number of photosynthetic electrons from the alga. They calculated this by comparing the number of electrons flowing through the circuit to the theoretical number that an untapped cell would use to generate oxygen under the same conditions. Improvements to electrode design should boost that figure, says Ryu.

Wim Vredenberg at the Wageningen University and Research Centre in the Netherlands has used similar techniques to study photosynthesis in algae. "[But] I never have thought of exploring electro-physiological technologies for harvesting the photoelectrons generated in chloroplasts," he says.

Biochemist James Barber at Imperial College London says the work is good, but that harvesting electrons in this way is impractical on a large scale. Using high-energy electrons that "leak" from some micro-organisms – a phenomenon exploited in microbial fuel cells – is more practical, he says.

"There is still a lot to do to make a practical system," concedes Ryu. "We thought of having an array of cantilevers that have multiple electrodes for a large-scale system," he says. Each electrode would pierce the chloroplast of a separate algal cell, held in an array of traps.

But one question remains unanswered. "We do not know for sure what effect this electron stealing will have on the life of the cells," says Ryu. "We want to keep them alive as long as possible."

Journal reference: Nano Letters, DOI: 10.1021/nl903141j

Early Dads Helped With Child Care, Researcher Suggests

Active fathers may have been a key factor in why our early ancestors were able to have many children, a study suggests.

By Josh Clark Wed Mar 17, 2010 08:21 AM ET

THE GIST:

**** Dads may have helped early humans have more children.***

**** Only 9 to 10 percent of all mammal species have males that help females raise their young.***

**** Early human ancestor dads may have helped with bathing and feeding of their kids.***

The males among our earliest human ancestors may have helped jumpstart the modern human population explosion by helping females with child rearing.

This paternal investment resembled the kind of hands-on parenting many dads still display, Northwestern University researcher Lee T. Gettler suggests in a new anthropological model of human evolution.

As there are in the modern era, there were some deadbeat dads who didn't lend a hand with child care in the distant past. "Other men might have been highly involved with direct care, engaging in behaviors not unlike what involved fathers do today," Gettler, a doctoral candidate at Northwestern, told Discovery News.

The study was published in the February issue of the journal American Anthropologist.

Dads in early human species would have aided in carrying children, as well as in their bathing, feeding, playing and teaching them the lessons of prehistoric life, said Gettler. They traded these services with the females for access to mating, allowing for monogamy and the modern family structure to develop.

Gettler's hypothesis aims to explain a mystery anthropologists have long explored. When the Homo genus branched off from other ape descendants, it grew larger by increasing caloric intake and reducing energy expenditures. The largest energy expenditures found in primate species is child-bearing and rearing.

Yet even as our pre-human ancestors grew larger, the amount of time between pregnancies -- known as the interbirth interval -- actually grew shorter than their smaller ancient counterparts. Females began having more, rather than fewer, children.

Gettler said the shorter interbirth interval and the long period of child rearing characteristic in modern humans could have only happened with ancient dads lending a hand.

With fathers helping to raise children, mothers didn't expend as much energy, leading to a shortened interbirth interval. As a result, the mothers reproduced more frequently.

Evolutionary biologist and biological anthropologist John Tooby of University of California at Santa Barbara agrees that fatherly care played a decisive role in human evolution. Yet Tooby, who is unaffiliated with Gettler's study, sees active fathers making humans a more dominant species not only because humans were able to reproduce more frequently, but because the additional care allowed us to develop better brains.

"Male provisioning allows more net parental care to go to infants, both during pregnancy and after birth, supporting a larger and more expensive brain, and a longer period of dependency," Tooby said. "So, certainly interbirth interval could shorten, but also infant quality can be heightened."

Josh Clark is a writer for HowStuffWorks.com.

New exoplanet like 'one of ours'

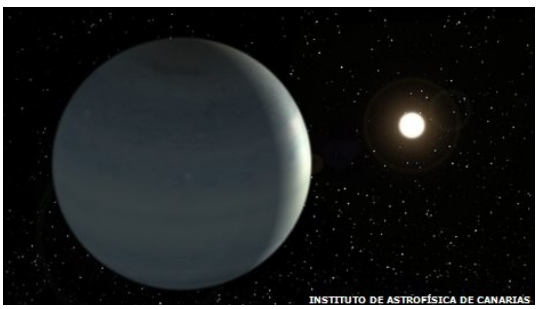
By Doreen Walton Science reporter, BBC News

It is 1,500 light-years from Earth but CoRoT-9b is the first temperate planet found known to be similar to those within our own Solar System.

The presence of CoRoT-9b was detected by a space mission designed to find planets we cannot see from the ground.

"It is the size of Jupiter and has an orbit similar to Mercury," said lead researcher Dr Hans Deeg.

In the journal Nature, the scientists say it is the first planet of its type which can yield detailed information.



An artists impression of CoRoT-9b which was spotted by the CoRoT satellite

Eccentric orbits

More than 400 exoplanets, or planets outside the Solar System, have been discovered so far but Dr Deeg, who works at the Instituto de Astrofisica de Canarias in the Canary Islands, explained that the others have all been "exotic".

"They are either extremely hot, being very close to the central star on short orbits, or they are on eccentric orbits, taking them close to and far from the central star, giving them extreme temperatures."

CoRoT-9b has a temperate climate. "This is the first planet where it makes sense to apply the models developed for planets within our solar system," said Dr Deeg.

The surface temperature is estimated to be between about -20 and 160 degrees Celsius.

Dr Deeg explained that although some of the exoplanets previously discovered were thought likely to be temperate it was not possible to confirm that or to find out much information about them.

The planet was discovered by an international team of 60 astronomers and identified using the "transit" method.

During its orbit of 95 days it passes in front of its central star, or transits, for about eight hours. "The transit method enables us to obtain much more information about it," explained Dr Deeg.

"We expect this to be a reference object for the next decade.

"We can derive its temperature as we know the distance to the central star and the type of central star it is."

A blue planet?

CoRoT-9b was spotted by the CoRoT satellite, which is a mission led by the French space agency, Centre National d'Études Spatiales. Its presence was then confirmed by observations from several telescopes from the European Southern Observatory, in Tenerife and at other sites.

"An analysis of the data from the satellite gives us the size and the data from the ground gives us the mass," explained Dr Deeg. "We don't know the colour. It's likely that it has high atmosphere water clouds which might make it blue but that depends on the mixture of gases which we really do not know," he added.

The scientists say the discovery of the planet shows that the development history of our Solar System has been repeated around other stars.

Targeting blood vessels, immune system may offer way to stop infection-caused inflammation

Protein pathway protects vessels from leaking fluid

SALT LAKE CITY - Treating virulent influenza, sepsis, and other potentially deadly infections long has focused on looking for ways to kill viruses and bacteria. But new research from the University of Utah and Utah State University shows that modulating the body's own overeager inflammatory response to infection may help save more lives.

In a study published March 17 in Science Translational Medicine, researchers led by U of U cardiologist Dean Y. Li, M.D., Ph.D., professor of internal medicine and director of the Molecular Medicine Program, shows that protecting blood vessels from hyper-inflammatory response to infection reduced mortality rates in mouse models of avian flu and sepsis by as much as 50 percent. Specifically, the researchers identified a protein signaling pathway, Robo4, that when activated prevents inflammation from weakening blood vessels, which causes them to leak and can result in life-threatening organ damage.

The findings raise the possibility of new broad-range therapies that could be rapidly implemented by public health agencies to fight both viral and bacterial infections, such as pandemic influenza and sepsis, and even potentially deadly human-made biological agents that could cause widespread illness and death, according to Li. Such therapies would be given along with antibiotics, antivirals, and other drugs.

"By blocking the ill effects of inflammation on the host or patient by stabilizing blood vessels, we have identified an entirely different strategy to treat these infections," Li said. "In essence, we've shown that rather than attacking the pathogen, we can target the host to help it to fight infections."

While this study proves the concept of controlling the effects of inflammation to fight the effects of serious infection, developing therapies for people will take years.

Inflammation is a powerful weapon in the body's immune system; without this inflammation, patients would not be able to fight infection. But it's also a double-edged sword. When Biochemical mediators, called cytokines, are released in massive quantities as part of the inflammatory response, they can destabilize blood vessels, resulting in leakage, tissue edema (swelling), and in extreme cases, organ failure and death. For example, a severe infection such as that of the 1918 pandemic flu, can cause life-threatening lung damage when alveoli become inflamed and fill with fluid, a condition known as lung edema. Similarly, sepsis can damage organs such as the kidneys by weakening blood vessels and allowing fluid to leak into the kidney tissue, impairing its vital functions.

Although it will take much more work to determine if Robo4 can be manipulated to block inflammation in sepsis, influenza, and other infections, the protein's signaling pathway appears to be ideal for stabilizing the endothelial cells that line blood vessels, according to Guy A. Zimmerman, M.D., a U of U professor of internal medicine who investigates inflammation and sepsis. "For this reason, the Robo4 pathway may be more effective and less likely to have negative side-effects than some of the approaches and drugs that have been tried in the past," said Zimmerman, a co-author on the study.

Targeting the pathogens that cause influenza and sepsis has been the primary strategy to fight those infections. While this has been successful, it also has limitations because pathogens can evolve quickly to develop resistance to antibiotics and antiviral medications. A second approach has been to dampen a patient's immune system response to infection. However, past approaches led to poor outcomes in patients, in part because they sometimes increased the sick individual's susceptibility to a second, "opportunistic" infection.

Protecting the host from its own inflammatory response to infection offers a potential strategy to reduce the mortality rate from many different types of serious infections. In the mouse models of this study, the mortality rate for some sepsis and avian flu infections approached 90 percent when left untreated. By protecting blood vessels through activating Robo4, mortality was reduced in some cases to almost half.

Dale L. Barnard, Ph.D., a virus specialist and research associate professor at the Institute for Antiviral Research in the Department of Animal, Dairy and Veterinary Sciences at Utah State University, said the study opens a potentially exciting approach to treating virulent viral-caused infections such as pandemic H1N1 and the highly infectious avian flu. "It may be even a more effective approach if it were to be used in combination with antiviral drug therapy, perhaps allowing the antiviral drug to be used at concentrations below those which would induce drug resistance or allow the drug to be administered for shorter periods of time," said Barnard, also a co-author on the study.

Li's study of Robo4 as an agent for mitigating the effects of inflammation grew from his research into blood vessel formation. In 2003, he cloned Robo4 and showed that it inhibits uncontrolled blood vessel growth, thereby stabilizing vessels and preventing leakage. Robo4 is activated by another protein, called Slit.

New Finding Puts Origins of Dogs in Middle East

By NICHOLAS WADE

Borrowing methods developed to study the genetics of human disease, researchers have concluded that dogs were probably first domesticated from wolves somewhere in the Middle East, in contrast to an earlier survey suggesting dogs originated in East Asia.

This finding puts the first known domestication - that of dogs - in the same place as the domestication of plants and other animals, and strengthens the link between the first animal to enter human society and the subsequent invention of agriculture about 10,000 years ago.

A Middle Eastern origin for the dog also fits in better with the archaeological evidence, and has enabled geneticists to reconstruct the entire history of the dog, from the first association between wolves and hunter gatherers some 20,000 years ago to the creation by Victorian dog fanciers of many of today’s breeds.

A research team led by Bridgett M. von Holdt and Robert K. Wayne of the University of California, Los Angeles, has analyzed a large collection of wolf and dog genomes from around the world. Scanning for similar runs of DNA, the researchers found that the Middle East was where wolf and dog genomes were most similar, although there was another area of overlap between East Asian wolves and dogs. Wolves were probably first domesticated in the Middle East, but after dogs had spread to East Asia there was a crossbreeding that injected more wolf genes into the dog genome, the researchers conclude in Thursday’s issue of the journal Nature.

The archaeological evidence supports this idea, since some of the earliest dog remains have been found in the Middle East, dating from 12,000 years ago. The only earlier doglike remains occur in Belgium, at a site 31,000 years old, and in western Russia from 15,000 years ago.

Humans lived as roaming hunters and gatherers for most of their existence. Dr. Wayne believes that wolves began following hunter-gatherer bands to feed on the wounded prey, carcasses or other refuse. At some stage a group of wolves, who happened to be smaller and less threatening than most, developed a dependency on human groups, and may in return have provided a warning system.

Several thousand years later, in the first settled communities that began to appear in the Middle East 15,000 years ago, people began intervening in the breeding patterns of their camp followers, turning them into the first proto-dogs. One of the features they selected was small size, continuing the downsizing of the wolf body plan. “I think a long history such as that would explain how a large carnivore, which can eat you, eventually became stably incorporated in human society,” Dr. Wayne said.

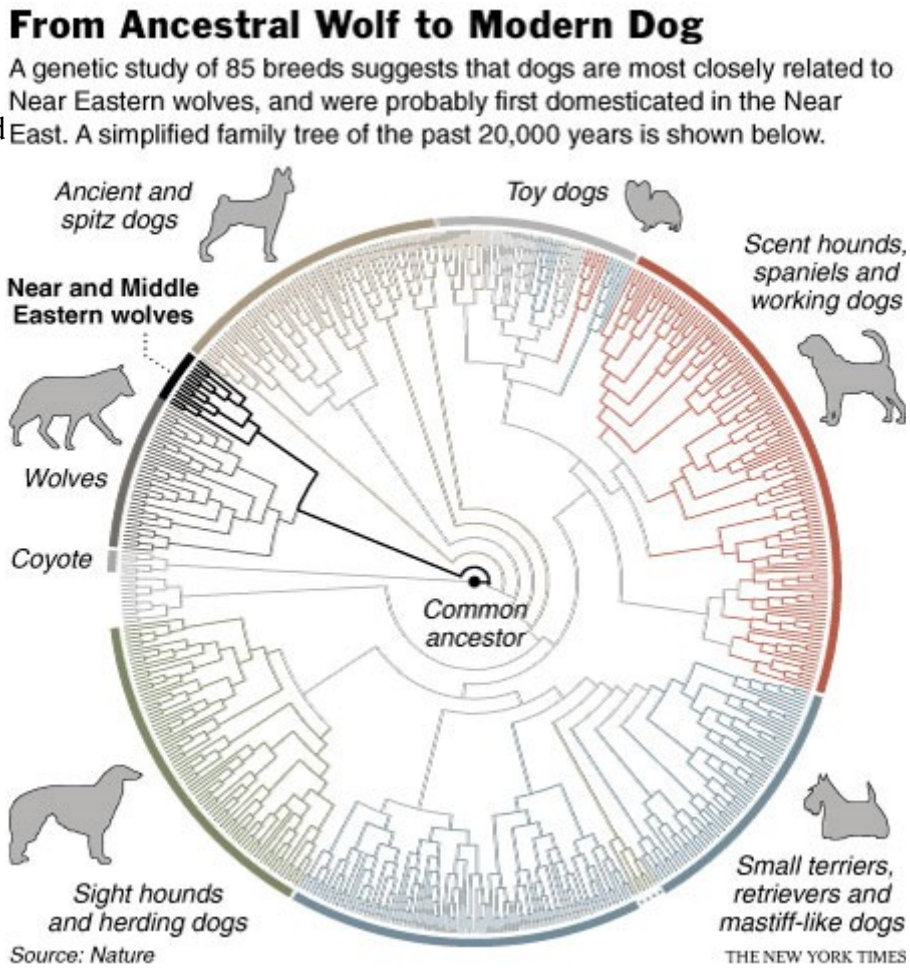
The wolf DNA in the study was collected over many years by Dr. Wayne from wolf packs around the world. A colleague, Elaine Ostrander, gathered much of the dog DNA by persuading owners at dog shows to let her

take a scraping of cells from inside the cheek. The dog genome has been decoded twice: scientists at the Broad Institute in Cambridge, Mass., have sequenced the boxer's genome, and Craig Venter, a pioneer of DNA sequencing, has decoded his poodle's genome.

With these two genomes in hand, the Broad Institute designed a dog SNP chip, similar to those used to scan the human for genetic disease. SNPs, or "snips," are sites of common variation along the DNA. Affymetrix, a SNP chip maker, manufactured the dog SNP chip for Dr. Wayne's team, letting him have 1,000 chips free, though thereafter they cost $250 apiece. The dog SNP chip brought to light the close relationship between dogs and wolves in the Middle East and also the genetic relationship between various breeds.

Dr. Wayne was surprised to find that all the herding dogs grouped together, as did all the sight hounds and the scent hounds, making a perfect match between dogs' various functions and the branches on the genetic tree. "I thought there would be many ways to build a herding dog and that they'd come from all over the tree, but there are not," Dr. Wayne said.

His team has also used the dog SNP chip to scan for genes that show signatures of selection. One such favored dog gene has a human counterpart that has been implicated in Williams syndrome, where it causes exceptional gregariousness. Another two selected genes are involved in memory. Dogs, unlike wolves, are adept at taking cues from human body language, and the two genes could have something to do with this faculty, Dr. Wayne said.



An earlier survey of dog origins, based on a small genetic element known as mitochondrial DNA, concluded that dogs had been domesticated, probably just once, in East Asia. The author of the survey, Peter Savolainen of the Royal Institute of Technology in Stockholm, said he was not convinced by the new report for several reasons, including that it did not sample dogs in East Asia from south of the Yangtze, the region where the diversity of mitochondrial DNA is highest. Also archaeologists in China have been less interested in distinguishing dog and wolf remains, he said.

Two other experts on dog genetics, Carlos Driscoll and Stephen O'Brien, of the National Cancer Institute, said they believed that Dr. Wayne's team had made a convincing case. "I think they have nailed the locale of dog domestication to the Middle East," Dr. O'Brien said in an e-mail message from Siberia, where he is attending a tiger management workshop.

Dog domestication and human settlement occurred at the same time, some 15,000 years ago, raising the possibility that dogs may have had a complex impact on the structure of human society. Dogs could have been the sentries that let hunter gatherers settle without fear of surprise attack. They may also have been the first major item of inherited wealth, preceding cattle, and so could have laid the foundations for the gradations of wealth and social hierarchy that differentiated settled groups from the egalitarianism of their hunter-gatherer predecessors. Notions of inheritance and ownership, Dr. Driscoll said, may have been prompted by the first dogs to permeate human society, laying an unexpected track from wolf to wealth.

France's national program to reduce HAIs reports important successes; uses mandatory reporting

Atlanta, GA - Researchers evaluating France's national infection control program for healthcare facilities found significant decreases in the rates of healthcare-associated infections (HAIs) since 2004. The drop in HAIs, including MRSA and surgical site infections, could be attributed to important changes in the national infection control system. France's national, regional and local coordinating centers have been reorganized to help

facilities throughout the country comply and conform with mandatory public reporting requirements and key program objectives. The findings were presented today at the Fifth Decennial International Conference on Healthcare-Associated Infections.

"The French National Program demonstrates the value of a national standard reporting system for healthcare-associated infections," said Neil Fishman, MD, President of SHEA. "As seen in this study, public transparency can lead to a culture of accountability and continuous healthcare quality improvement. Having accurate data for action drives progress toward the elimination of HAIs, but we need the appropriate infrastructure to achieve these goals."

Laetitia May-Michelangeli, MD Ministry of Health & Sports (MoH), and Christian Brun-Buisson, MD, chair of the national infection control program at Hospital Henri Mondor in Paris, worked with a team of infection control experts to evaluate the impact of the national program to reduce HAIs.

Researchers evaluated aggregated data compiled from mandatory annual reports by national surveillance networks from 2005 through 2008. A random sampling of the facilities' annual reports was verified through auditing by subsidiaries from the MoH. "Many of the target objectives have been achieved," said Dr. May-Michelangeli. "Most healthcare facilities (89 percent) have reached the best performance class for the global indicator of HAI control based on facility type, resources and activities."

The findings are extracted from mandatory reporting records to the MoH. Every healthcare facility registered at the MoH has to provide an annual report on infection prevention programs. From these reports, researchers analyzed data from 2,800 facilities including large university hospitals, ambulatory care, long-term care or small community clinics.

"The national mandatory public reporting system has helped healthcare facilities to improve their infection control measures," said Dr. Brun-Buisson. "Not only do these facilities have funding tied to their compliance with the program, but the media in France now publish a list of best and worst performing hospitals based on each facility's annual report."

The French National Program also looked to promote other priority initiatives to reduce HAIs, including advancing new research in the field, improving communication with patients on the risk of infectious diseases, standardizing monitoring methods for HAIs and adopting preventive practices for healthcare professionals.

Key achievements of the program include:

* MRSA cases have decreased by 40 percent;
* Local and regional infection control teams have been appointed in 94 percent healthcare facilities;
* The use of alcohol-based products for hand hygiene doubled in over 50 percent of the sites;
* Nearly all (90 percent) of the facilities have implemented an evaluation program and a system for quickly disseminating infection alerts (96 percent);
* Most facilities (89 percent) have an anti-infective drug committee and have produced guidelines for preventing surgical site infections (97 percent);
* Many facilities (88 percent) follow-up with patients' antibiotic consumption; and
* Nearly all facilities (98 percent) provide patients an information leaflet on HAIs.

While France's healthcare system is different from the U.S., researchers believe that reducing HAIs through public reporting can be successfully applied to any healthcare system. To further the goal of improving country-wide control of HAIs, MoH has initiated a second phase of the program that will continue through 2013. This phase includes revised national infection prevention and control objectives and goals for individual healthcare facilities. *For further information on the Fifth Decennial, or to register to attend, please visit: www.decennial2010.org.*

How to move the brain with a Japanese line drawing

* 18 March 2010 **by Wendy Zukerman**

Gallery: Art through instability: how drawings move the brain

IN THE YouTube age it is easy to forget that artists rely on clever tricks to create a sense of motion in still images. Now brain scans show why one method of creating "implicit motion", used by an 18th-century Japanese artist, works so well.

While admiring line drawings by Hokusai Katsushika, psychophysicist Naoyuki Osaka of Kyoto University, Japan, was struck by the vivid motion they convey. Instead of using blur to suggest movement, as much modern art has done since the advent of photography, Katsushika created motion by drawing bodies in highly unstable positions (see picture). This is thought to work because the brain "fills in" the effects of gravity pulling the bodies down.

Previous research has shown that blurred photographs stimulate the same regions of the visual cortex as real-life motion, including the extrastriate visual cortex. To find out whether sketches of unstable bodies would also

activate these regions, Osaka showed Japanese students Katsushika's drawings while scanning their brains with functional MRI.

The scans revealed that drawings depicting motion did indeed prompt activity in the extrastriate visual cortex, unlike those of people or objects in static positions. Osaka concludes that there is a "common neural pathway" for interpreting implicit motion in art that is similar to the pathway used for perceiving real-life motion (NeuroReport, DOI: 10.1097/wnr.0b013e328335b371).

Patrick Johnston, a cognitive neuroscientist at Swinburne University of Technology in Melbourne, Australia, says these findings could help "unlock how the brain processes visual information".

However, Oron Catts of SymbioticA, a biological arts centre at the University of Western Australia in Perth, warns that the influence of culture must not be ignored. Japanese people may perceive the motion more vividly than people from other cultures because they are accustomed to this type of art, he suggests. "In Japanese culture, people are trained to read those cartoon images as the representation of movement."

Why do we seem to be moving? **(Image: Hokusai Katsushika (1878), reproduced on microfilm by Adam Matthew Publications/Bodleian Photographic Service/National Library of Australia)**

Breakthrough for babies born with severe cleft palates after experiments at ISIS

Scientists working on a treatment for babies born with cleft palates have made a promising breakthrough and the first clinical trials are planned for early next year. Clefts are the most common birth defect in Britain, with one in every 700 babies affected; currently in severe cases radical surgery is required to correct the problem, and in addition future complications can occur as the child grows into an adult. The preliminary results on a hydrogel material studied using the Science and Technology Facilities Council's ISIS neutron source show treatment for severe cleft palates could be carried out without the need for complex surgery.

Cleft palates are currently repaired by surgically repositioning the available palatal mucosa, the tissue structure at the roof of the mouth, in order to cover the gap in the palate. However, if the cleft defect is too wide there may be insufficient local tissue available to close the gap without undertaking quite radical surgery. It is these severe cases that can cause future complications for infants as they develop into adults – particularly with speech and facial growth problems.

A team of researchers at the University of Oxford, the John Radcliffe Hospital in Oxfordshire, and the Georgia Institute of Technology in the United States has used ISIS to look at hydrogel on the molecular level to try and gather enough information to develop materials that could be used for a potential new treatment.

"ISIS provided us with the high level of structural detail we needed to assess the new material. It gives unique and accurate results that we can't get with any other technique," says Professor David Bucknall from the Georgia Institute of Technology.

The new potential treatment for these severe cases involves inserting a small plate made of an anisotropic hydrogel material (similar to that used in contact lenses) under the mucosa of the roof of the mouth of the patient.

The hydrogel gradually expands as fluid is absorbed, encouraging skin growth over and around the plate – a process known as 'tissue expansion'. When sufficient skin has been generated to repair the palatal cleft, the plate is removed and the cleft is repaired by using this additional tissue. The success of the preliminary results of self-inflating anisotropic hydrogel tissue expanders mean clinical trials in this area are expected to take place early in 2011.

"Babies born with cleft palates usually have problems feeding, and may have speech difficulties in later life, as well as issues with their hearing, dentition and facial growth," says Mr Marc Swan a plastic surgeon at the John Radcliffe Hospital in Oxford, and the instigator of the study. "The severest cases often have the least favourable outcomes and unfortunately these are the most challenging children to treat surgically."

Rosanna Preston, CEO of CLAPA (The Cleft Lip and Palate Association) commenting on the research said; "Facial clefts of the lip or palate are the most common birth defect and it is vital that we continue to explore new treatments to help those affected. This research is particularly interesting as it addresses the most severe cases where the effects on the child's development may be greatest. We will be excited to see the results of the clinical trials."

The study is the first to be carried out using the Offspec instrument at the recently opened second target station at ISIS. Offspec is the world's most advanced neutron instrument for studying new surface structures

and can be used for a number of applications including biological membranes and patterned materials for data storage media.

Andrew Taylor, ISIS Director says: "This study shows how fundamental knowledge about the structure of materials can be used to develop new technology. The instruments at the new ISIS second target station build on 25 years of expertise developed in the UK. They are designed to allow new areas of research to flourish – particularly in soft matter and bioscience – and make it easy for research teams to get the important results that they need. We're pleased that at ISIS we can continue to contribute to research affecting everyday lives."

Post-coital warfare: insect semen kills rival sperm

* 18:00 18 March 2010 **by Wendy Zukerman**

If you've only got one shot, you better make it count. For some social insects, with only one chance to impregnate their queen, things can get nasty, but it's not the males that try to harm each other: it's their ejaculate.

Some female insects, such as honeybees and leafcutter ants, have sex on only one day in their life. But what a day: they mate with multiple males and store enough sperm to fertilise eggs throughout their lives.

Now it seems that when honeybees and leafcutter ants inseminate the queen, their seminal fluid is harmful to rival sperm. Researchers looking at sexual selection often focus on the all-important sperm, says Boris Baer of the University of Western Australia. The seminal fluid tends to be discounted as merely a sugary liquid which provides energy, he says.

Baer and colleagues from the University of Copenhagen, Denmark, exposed the sperm of honeybees and leafcutter ants to their own seminal fluid, and the secretions of other males of the same species. The seminal fluid killed more than 50 per cent of the rival sperm within 15 minutes. "The males seemed to use the seminal fluid to harm the sperm," says Baer.

One chance to mate

The team repeated the experiment with species that only mate once in their life such as bumblebees (Bombus terrestris) and Trachymyrmex ants. As expected the seminal fluid of these strictly monandrous species, which never encounters the sperm of a competitor, didn't assault alien sperm.

The seminal fluid of the polyandrous species also protected and increased the survival rate of their own sperm, says Baer – which implies that like the immune system of vertebrates there is something in the seminal fluid that recognises "self" and "non-self". "That is a weird idea," says Baer, "that fluid is capable of doing that."

Females also put up a fight to save the sperm inside them. Baer and colleagues found that queen leafcutter ants can chose to secrete a fluid that protects sperm from the damaging effects of seminal fluid from rival males.

Strongest sperm win

"The queens can let the warfare run as long as she wants," says Baer, who believes the female could wait for the strongest sperm to survive the attacks before releasing her fluid to ensure she maintains enough viable sperm to fertilise all eggs needed to run a colony.

So, could we imagine a similar substance found within human seminal fluid?

"To my knowledge women do not copulate with 90 mates in half an hour, so whether there is much room that this has evolved in humans as well, I have my doubts," says Baer. But he's not ruling it out: "In the sperm world you must be prepared for everything.

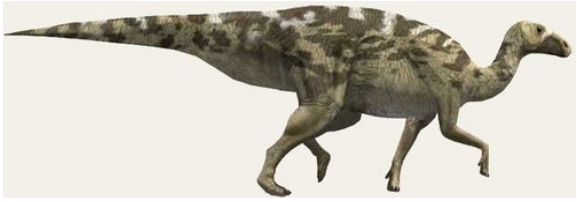
Bryan Fry, an insect biologist at the University of Melbourne, Australia, is impressed." When it comes to the battle for insemination, Fry says, "It is always fascinating to see the techniques used by animals to reinvent the wheel." *Journal reference: Science, DOI: 10.1126/science.1184709*

Dinosaurs Did Not Gradually Die Out

By Jennifer Viegas Thu Mar 18, 2010 03:51 PM ET

Non-avian dinosaurs became extinct 65 million years ago, and now researchers have proven that this die-off didn't happen over a long period of time.

A detailed look at dinosaur bones, tracks and eggs located at 29 archaeological sites located in the Catalan Pyrenees reveals that there was a large diversity of dinosaur species living there just before the fatal K-T extinction event, which many scientists believe was caused by several large meteors hitting Earth.



Parahabdodon isonensis, one of the Catalan dinosaurs; **Credit: Violeta Riera, Autonomous University of Barcelona**

Dinosaurs thrived outside of this part of Spain as well before 65 million years ago, such as in North America, but this particular research, published in the journal Palaeogeography, Palaeoclimatology, Palaeoecology, focused on the Catalan region, a former dinosaur hotbed.

Sites at towns like Tremp and Aren are rich in dinosaur bones, while those in Vallcebre contain many dinosaur tracks. Excavations at the town of Coll de Nargó have also unearthed many fossilized dinosaur eggs. These date to the Maastrichtian, the last stage of the Cretaceous period. The researchers could even see incredible dino diversification in the upper layers of the Maastrichtian, just before non-avian dinosaurs disappeared off the face of the planet.

The research also shows for the first time that the Sauropod titanosaurus (an herbivorous quadruped that grew to enormous sizes), as well as the nodosaurid dinosaurs (armoured herbivores), preferred swampy habitats, while other dinosaurs such as the dromaeosaurids (relatively small-sized carnivores, closely related to birds) lived in practically all types of environments.

For the Autonomous University of Barcelona's Violeta Riera, who worked on the project, studying dinosaurs in Catalonia is a privilege, given that “the dinosaurs found here are the last specimens that lived on Earth."

“The Pyrenees," she affirms, “are the only place in Europe where quality research can be carried out on the period in which they became extinct." No other European mountain range offers such rich sites since “at that time, Europe was a large archipelago with not much land for dinosaurs."

Women do make men throw caution to the wind, research confirms

SPPS research on testosterone levels and risk-taking in young men

Los Angeles, CA - The presence of an attractive woman elevates testosterone levels and physical risk taking in young men, according to a recent study in the inaugural issue of Social Psychological and Personality Science (published by SAGE).

Researchers asked young adult men to perform both easy and difficult tricks on skateboards, first in front of another male and then in front of a young, attractive female. The skateboarder's testosterone levels were measured after each trick.

When skateboarders attempt tricks, they make a split-second decision about whether to abort the trick or try to land it, based on a mid-air evaluation of the likelihood of success and on the physical costs that failure might bring. It was that moment the researchers sought to examine because it resembles the type of risky decisions that young men make when behind the steering wheel of a car or when in physical confrontations with each other.

Consistent with predictions, the young men took greater risks in the presence of the attractive female even when they knew there was a greater chance that they would crash. Testosterone levels were significantly higher in these men than in the men who were in the presence of another male.

"This experiment provides evidence for an effect that has existed in art, mythology, and literature for thousands of years: Beautiful women lead men to throw caution to the wind," write authors Richard Ronay and William von Hippel. "These findings suggest that, for men, the adaptive benefits gained by enticing mates and intimidating rivals may have resulted in evolved hormonal and neurological mechanisms that facilitated greater risk taking in the presence of attractive women."

The article "The presence of an attractive woman elevates testosterone and physical risk taking in young men" in Social Psychological and Personality Science is available free for a limited time at http://spp.sagepub.com/cgi/reprint/1/1/57.

Deep Brain Stimulation May Help People With Epileptic Seizures

Epilepsy Experiment Involves Risky Surgery, but Helps Serious Cases; FDA Approval Urged

By JOSEPH BROWNSTEIN and DAN CHILDS ABC News Medical Unit

March 18, 2010 - Stephen Neiley's first seizure happened when he was 39 years old, while he was having dinner with his family. It would be far from his last.

From then on, for the next 13 years, Neiley, a former San Diego contractor, would have a grand mal seizure -- in which a person loses consciousness and has violent muscle contractions -- every two to three days. He would have petit mal seizures -- in which one seems to freeze for a few seconds -- every other day. Treatment with drugs did not work. He said he had surgery that removed about one-third of his brain tissue, but the seizures continued. Diagnosed with epilepsy, returned to his hometown of Towanda, Pa.

"When it started, I had to give up everything, and I had to move back here," he said. "I had grand mal seizures. I had petit mal seizures. They became out of control."

But Neiley, now 57, says an invasive and risky but promising procedure has given him his life back.

Five years ago, he had a deep brain stimulation device implanted in his head by Dr. Michael Kaplitt at Weill Cornell Medical College in New York. He said the device, normally associated with treatment for Parkinson's disease, has greatly reduced the seizures that had ruled his life.

"I have about one seizure every month now, and that's at night, when I'm asleep," he said. "I have not had one during the day now for over five years."

Today, Kaplitt is part of a large group of researchers announcing the successful results of a double-blind, randomized trial of deep brain stimulation trial for epilepsy. The findings of the trial were published Thursday in the journal Epilepsia.

The trial involved implanting an electrical stimulation device in 110 patients. For the first three months, half had the devices activated. After that period, for the remaining nine months, all patients received mild electrical stimulation. Patients were followed up on for two years.

Researchers report that 54 percent of patients had the frequency of their seizures cut in half, and 14 patients were seizure-free for five months.

This new study "provides very objective support for the idea that this is effective," said Kaplitt. "I think that what this provides is a new type of weapon in the battle against seizures, and it provides legitimate hope to people who may have had no hope." He said that some patients are able to be treated very effectively with drugs and other more conventional approaches, but "then you have patients whose lives are being devastated. This disease is not being adequately controlled, and their lives are being ruined."

Deep brain stimulation has been previously approved for Parkinson's disease and movement disorders. In addition to epilepsy, it is being considered for depression.

A U.S. Food and Drug Administration advisory panel recommended that the agency approve deep brain stimulation as a treatment for epilepsy on March 12, but a final decision has not been made.

Deep Brain Stimulation: Not For Everyone

While the trial appears promising, doctors caution that deep brain stimulation is not for most people with epilepsy.

Dr. Tallie Baram, a pediatric neurologist and epilepsy researcher at the University of California - Irvine said only a third of people with epilepsy do not respond to medications. In some of those patients, the cause of epilepsy can be explained by a lesion in the brain. If the lesion is in an area that can be operated on, it may be removed and possibly help with the seizures.

For patients who cannot be helped by this, deep brain stimulation becomes a potential option.

"It can be a very terrible disease when it does not respond to medication," said Baram.

And that is when the risk-benefit ratio might change enough to make something like deep brain stimulation worthwhile. "It is very invasive; you need to go into people's brains and put in wires," she said. There are risks of hemorrhage and infection, although neither occurred during this trial. "It's expensive, it's invasive, it's dangerous long-term, so it's not something you think lightly about."

This study, she said, will give doctors confidence when considering deep brain stimulation as an option for their patients. "This is a [beautifully] designed study. Clearly this is an invasive procedure, and when implemented it should be done in the very careful manner done here."

Dr. Matt Stead, a pediatric neurologist at the Mayo Clinic, cautioned that for the time being, the treatment should be reserved for patients with the worst cases of untreatable seizures.

"These patients, we really don't have a lot to offer them. If we could decrease their seizures by 50 percent, that's really a big improvement for them."

A Different Life

As for Neiley, he now lives on a 100-acre piece of land along the Susquehanna River. It's a different lifestyle, he said. But now that his seizures are gone, he says he enjoys the change. "Since the day they did it until today, I'm an entirely different person," he said. "It has solved a lot of problems for me. I have a better life."

He said he would urge other patients who are facing what he faced to explore their options with deep brain stimulation. “I would tell them to go talk to their doctor about it... I've tried a lot of different things, and this is the best I've had."

Study shows further benefits of noscapine for prostate cancer

Baltimore, MD. – New research has revealed a major breakthrough in the use of cough medicine ingredient noscapine as a prophylactic treatment for prostate cancer. The study shows that noscapine inhibited tumor growth in mice and also limited the spread of tumors without causing any side effects.

The collaborative pre-clinical laboratory research was conducted by Dr. Israel Barken, of the Prostate Cancer Research and Education Foundation (PCREF), Moshe Rogosnitzky, of the MedInsight Research Institute and Dr. Jack Geller, of the University of California San Diego.

They concluded that noscapine administered as a preventive measure may offer significant benefits in the management of prostate cancer, a disease that kills more than 28,000 men in the U.S. each year.

Their findings said: "Pre-treatment with noscapine confers a significant benefit compared with control in both primary tumor growth and primary tumor growth- inhibition rate and exhibits an extremely favorable tolerability profile."

The research team is now keen to take their work further by examining the effects of noscapine – a non-addictive derivative of opium – as a prophylactic agent given to patients following prostate cancer surgery or radiation.

Dr. Barken, Founder and Medical Director of the PCREF in San Diego, California, said: "PCREF is now seeking sponsorship for clinical data collection in post-surgery patients who are at high-risk of recurrence for their prostate cancer.

"Based on our research so far, we believe that noscapine could be a very promising treatment to prevent recurrence in such cases due to its excellent safety record and oral bioavailability."

The latest research focused on pre-treating mice with noscapine before injecting them with prostate cancer cells. This resulted in the tumor growth rate being two-thirds smaller in the noscapine group compared with a non-noscapine group. The study also found that lung metastasis rates were 80% less in the mice pre-treated with noscapine, while the experts noted that the noscapine group suffered no cancer-related weight loss – compared with significant weight loss in the non-noscapine group.

Noscapine has been used worldwide since the 1950s as an ingredient in over-the-counter cough medicines and was originally suggested as an anti-cancer agent in the early 1960s. But major studies of its anti-cancer properties have only taken place in recent years.

The latest research is the result of ongoing collaborative work between the Prostate Cancer Research and Educational Foundation (PC-REF) and Baltimore-based MedInsight Research Institute. Their previous work has shown that noscapine has properties that limit the growth of prostate cancer.

The latest study was based on the theory that prostate cancer could be a suitable target for a risk-reduction approach because of its high prevalence and significant morbidity and mortality.

Moshe Rogosnitzky, co-founder and Director of Research at the MedInsight Research Institute, said: "There is an ever-growing need for effective ways to prevent recurrence of cancer after curative surgery.

"It is MedInsight's belief that many effective treatments for this and other diseases can be selected from the vast armory of existing off-patent and unpromoted drugs. The results of this study, once confirmed in a clinical trial, are an example where we may yet again have an agent that not only has an envious safety record, but is already available for use today."

The findings of the pre-clinical study are published in Anticancer Research (Volume 30:2, 2010, pp. 399-402) on March 19 2010.

Why teenagers find learning a drag

* 14:09 19 March 2010 **by Jessica Hamzelou**

Being a teenager can be a drag. As if dealing with peer pressure and raging hormones weren't hard enough, your ability to learn new things is also reduced. Now the brain molecules behind this learning deficit have been identified in mice - and blocked.

When children hit puberty, their ability to learn a second language drops, they find it harder to learn their way around a new location and they are worse at detecting errors in cognitive tests.

Why is this? Sheryl Smith and her colleagues at the State University of New York now reckon that all of these behavioural changes could be due to a temporary increase in a chemical receptor that inhibits brain activity in an area responsible for learning.

In 2007, Smith's team discovered that the number of these receptors soared in mice when they hit puberty, before falling back in adulthood. In their latest study, Smith's team set about finding out if these receptor changes in mice might lead to impaired learning abilities, rather like those seen in pubescent humans.

Shocking memory

The group examined the hippocampus – a region known to be involved in learning – in mouse brains. Sure enough, pubertal mice had seven times as many of the receptors as infant mice. In adulthood, the number of these receptors fell back to an intermediate level.

The team was also able to examine individual neurons and could see that the extra receptors were being expressed specifically at "neural projections" – sites within the hippocampus known to be involved in learning. This was further evidence that the increase in receptors might affect learning.

Finally, the group measured spatial learning abilities in the mice. The creatures were placed on a rotating platform, on which a stationary section delivered a mild electric shock. After a single shock, the infant mice learned to dodge the danger zone. The pubertal mice, however, failed to learn to avoid it even after several rounds.

Smith reckons that the same mechanism might underlie the learning deficits teenagers experience. Cheryl Sisk at Michigan State University at East Lansing agrees that "mouse puberty is similar to human puberty, although the timescale is different".

Learning restored

"The research adds to the growing body of literature indicating that puberty and adolescence are a unique period of nervous system development," says Sisk. "Adolescents aren't just in between children and adults. Their behaviour is different from both."

In a further experiment, Smith found that she could remove the learning deficit by injecting pubertal mice with THP – a stress steroid. In children and adult humans, THP is naturally released in response to stress. It reduces brain activity and calms you down, says Smith. But in pubertal mice, THP has the opposite effect – increasing their stress.

Smith suggests that in her most recent experiment, giving extra THP to pubertal mice similarly increased their brain activity and that this activity may have compensated for their learning deficits.

If similar mechanisms underlie teenage learning deficits in humans, this result might point to ways to deal with them - either through behavioural changes or drugs.

Smith suggests that a synthetic form of THP could be developed for teenagers with learning difficulties, although she acknowledges that care would need to be taken not to create any new problems. "We would have to be careful not to affect their mood," she says.

Sisk cautions that it's too soon to apply the results to humans or to other types of learning outside the spatial type tested in the mice. *Journal reference: Science, DOI: 10.1126/science.1184245*

Acne Drug Prevents HIV Breakout

Johns Hopkins scientists have found that a safe and inexpensive antibiotic in use since the 1970s for treating acne effectively targets infected immune cells in which HIV, the virus that causes AIDS, lies dormant and prevents them from reactivating and replicating.

The drug, minocycline, likely will improve on the current treatment regimens of HIV-infected patients if used in combination with a standard drug cocktail known as HAART (Highly Active Antiretroviral Therapy), according to research published now online and appearing in print April 15 in The Journal of Infectious Diseases. “The powerful advantage to using minocycline is that the virus appears less able to develop drug resistance because minocycline targets cellular pathways not viral proteins,” says Janice Clements, Ph.D., Mary Wallace Stanton Professor of Faculty Affairs, vice dean for faculty, and professor of molecular and comparative pathobiology at the Johns Hopkins University School of Medicine.

“The big challenge clinicians deal with now in this country when treating HIV patients is keeping the virus locked in a dormant state,” Clements adds. “While HAART is really effective in keeping down active replication, minocycline is another arm of defense against the virus.”

Unlike the drugs used in HAART which target the virus, minocycline homes in on, and adjusts T cells, major immune system agents and targets of HIV infection. According to Clements, minocycline reduces the ability of T cells to activate and proliferate, both steps crucial to HIV production and progression toward full blown AIDS.

If taken daily for life, HAART usually can protect people from becoming ill, but it’s not a cure. The HIV virus is kept at a low level but isn’t ever entirely purged; it stays quietly hidden in some immune cells. If a person stops HAART or misses a dose, the virus can reactivate out of those immune cells and begin to spread.

The idea for using minocycline as an adjunct to HAART resulted when the Hopkins team learned of research by others on rheumatoid arthritis patients showing the anti-inflammatory effects of minocycline on T cells. The Hopkins group connected the dots between that study with previous research of their own showing that minocycline treatment had multiple beneficial effects in monkeys infected with SIV, the primate version of HIV. In monkeys treated with minocycline, the virus load in the cerebrospinal fluid, the viral RNA in the brain and the severity of central nervous system disease were significantly decreased. The drug was also shown to affect T cell activation and proliferation.

“Since minocycline reduced T cell activation, you might think it would have impaired the immune systems in the macaques, which are very similar to humans, but we didn’t see any deleterious effect,” says Gregory Szeto, a graduate student in the Department of Cellular and Molecular Medicine working in the Retrovirus Laboratory at Hopkins. “This drug strikes a good balance and is ideal for HIV because it targets very specific aspects of immune activation.”

The success with the animal model prompted the team to study in test tubes whether minocycline treatment affected latency in human T cells infected with HIV. Using cells from HIV-infected humans on HAART, the team isolated the “resting” immune cells and treated half of them with minocycline. Then they counted how many virus particles were reactivated, finding completely undetectable levels in the treated cells versus detectable levels in the untreated cells.

“Minocycline reduces the capability of the virus to emerge from resting infected T cells,” Szeto explains. “It prevents the virus from escaping in the one in a million cells in which it lays dormant in a person on HAART, and since it prevents virus activation it should maintain the level of viral latency or even lower it. That’s the goal: Sustaining a latent non-infectious state.”

The team used molecular markers to discover that minocycline very selectively interrupts certain specific signaling pathways critical for T cell activation. However, the antibiotic doesn’t completely obliterate T cells or diminish their ability to respond to other infections or diseases, which is crucial for individuals with HIV.

“HIV requires T cell activation for efficient replication and reactivation of latent virus,” Clement says, “so our new understanding about minocyline’s effects on a T cell could help us to find even more drugs that target its signaling pathways.” *The research was supported by grants from the National Institutes of Health.*
Authors of the paper, in addition to Clements and Szeto, are Angela K. Brice, Sheila A. Barber and Robert F. Siliciano, all of Johns Hopkins. Also, Hung-Chih Yang of National Taiwan University Hospital.
On the Web: *http://www.hopkinsmedicine.org/mcp/faculty_webpages/clements.html*
http://www.hopkinsmedicine.org/mcp/Retrovirus/ *http://www.journals.uchicago.edu/toc/jid/current*
Related Video: *http://www.youtube.com/watch?v=C_ImNAEpOHY*
Janice E. Clements, Ph.D., on her teams discovery that a safe, inexpensive antibiotic will improve on the current treatment regimens of HIV-infected patients.

Seaweed to tackle rising tide of obesity

Seaweed could hold the key to tackling obesity after it was found it reduces fat uptake by more than 75 per cent, new research has shown. Now the team at Newcastle University are adding seaweed fibre to bread to see if they can develop foods that help you lose weight while you eat them. A team of scientists led by Dr Iain Brownlee and Prof Jeff Pearson have found that dietary fibre in one of the world's largest commercially-used seaweed could reduce the amount of fat absorbed by the body by around 75 per cent.

The Newcastle University team found that Alginate – a natural fibre found in sea kelp – stops the body from absorbing fat better than most anti-obesity treatments currently available over the counter.

Using an artificial gut, they tested the effectiveness of more than 60 different natural fibres by measuring the amount of fat that was digested and absorbed with each treatment.

Presenting their findings today at the American Chemical Society Spring meeting in San Francisco, Dr Brownlee said the next step was to recruit volunteers and study whether the effects they have modelled in the lab can be reproduced in real people, and whether such foods are truly acceptable in a normal diet.

"The aim of this study was to put these products to the test and our initial findings are that alginates significantly reduce fat digestion," explains Dr Brownlee.

"This suggests that if we can add the natural fibre to products commonly eaten daily - such as bread, biscuits and yoghurts – up to three quarters of the fat contained in that meal could simply pass through the body. "We have already added the alginate to bread and initial taste tests have been extremely encouraging. Now the next step to to carry out clinical trials to find out how effective they are when eaten as part of a normal diet."

The research is part of a three year project being funded by the Biotechnology and Biological Sciences Research Council. It addresses the new regulations set out by the European Food Safety Authority that any health claims made on a food label should be substantiated by scientific evidence.

"There are countless claims about miracle cures for weight loss but only a few cases offer any sound scientific evidence to back up these claims," explains Dr Brownlee.

Alginates are already commonly used at a very low level in many foods as thickeners and stabilisers and when added to bread as part of a blind taste test, Dr Brownlee said the alginate bread actually scored higher for texture and richness than a standard white loaf.

"Obesity is an ever-growing problem and many people find it difficult to stick to diet and exercise plans in order to lose weight," explained Dr Brownlee. "Alginates not only have great potential for weight management - adding them to food also has the added advantage of boosting overall fibre content."

What is a dietary fibre?

Dietary fibre would be scientifically classified as a group of carbohydrates of plant origin that escape digestion by the human gut. "Actually, there's still quite a lot of confusion about fibre," says Dr Brownlee. "I think most people would describe it as roughage – the bit of your food that keeps you regular and is vital for a healthy gut.

"Both of these facts are true but the notion that all fibre is the same and that it simply goes through your system without having an effect is wrong."

Fibre is made up of a wide range of different molecules called polysaccharides and although it is not digested by the human gut, it both directly and indirectly affects a number of bodily processes. Dr Brownlee adds: "These initial findings suggest alginates could offer a very real solution in the battle against obesity."

Newly identified growth factor promotes stem cell growth, regeneration

DURHAM, N.C. - Scientists at Duke University Medical Center have identified a new growth factor that stimulates the expansion and regeneration of hematopoietic (blood-forming) stem cells in culture and in laboratory animals. The discovery, appearing in the journal Nature Medicine, may help researchers overcome one of the most frustrating barriers to cellular therapy: the fact that stem cells are so few in number and so stubbornly resistant to expansion.

Researchers believe that umbilical cord blood could serve as a universal source of stem cells for all patients who need a stem cell transplant, but the numbers of stem cells in cord blood units are limited, so there is a clinical need to develop a method to expand cord blood stem cells for transplantation purposes. "Unfortunately, there are no soluble growth factors identified to date that have been proven to expand human stem cells for therapeutic purposes," said John Chute, M.D., a stem cell transplant physician and cell biologist at Duke and senior author of the paper.

Chute, working with Heather Himburg, a post-doctoral fellow in his laboratory, discovered that adding pleiotrophin, a naturally-occurring growth factor, stimulated a ten-fold expansion of stem cells taken from the bone marrow of a mouse.

They also found that pleiotrophin increased the numbers of human cord blood stem cells in culture that were capable of engraftment in immune-deficient mice. When they injected pleiotrophin into mice that had received bone marrow-suppressive radiation, they observed a 10-fold increase in bone marrow stem cells compared to untreated mice. "These results confirmed that pleiotrophin induces stem cell regeneration following injury," said Chute.

Chute says the finding could lead to broader application of cord blood transplants for the large numbers of patients who do not have an immune-matched donor "Perhaps more importantly, systemic treatment with pleiotrophin may have the potential to accelerate recovery of the blood and immune system in patients undergoing chemotherapy or radiotherapy," he said.

Given the potency of the effect of pleiotrophin on stem cell expansion, the authors examined whether pleiotrophin provoked blood-forming cells to become malignant. So far, Chute says they have not seen any evidence of cancer in mice up to six months after treatment with pleiotrophin.

The Duke team is already conducting further experiments to determine if pleiotrophin is necessary for normal stem cell growth and development, and Chute says it will be important to conduct additional animal studies before moving into human clinical trials. "At this point, any progress we can make that helps us better understand which biological pathways are activated in stem cells in response to pleiotrophin will help move the discovery forward." *A grant from the National Institutes of Health supported the study.*
Co-authors from Duke who contributed to the work include Pamela Daher, Sarah Meadows, Lauren Russell, Phuong Doan, Jen-Tsan Chi, Alice Salter, William Lento, Tannishtha Reya and Nelson Chao.

Einstein researchers discover 2 new ways to kill TB

Findings could help tame extremely drug-resistant strains

BRONX, NY - Researchers at Albert Einstein College of Medicine of Yeshiva University have found two novel ways of killing the bacteria that cause tuberculosis (TB), a disease responsible for an estimated two million deaths each year. The findings, published in the March 21 online issue of Nature Chemical Biology, could lead to a potent TB therapy that would also prevent resistant TB strains from developing.

"This approach is totally different from the way any other anti-TB drug works," says William R. Jacobs, Jr., Ph.D., the study's senior author and professor of microbiology & immunology and of genetics at Einstein, as well as a Howard Hughes Medical Institute investigator. "In the past few years, extremely drug resistant strains of TB have arisen that can't be eliminated by any drugs, so new strategies for attacking TB are urgently needed."

Tuberculosis is caused by the bacterial species Mycobacterium tuberculosis. In searching for a new Achilles' heel for M. tuberculosis, Dr. Jacobs and colleagues focused on an enzyme called GlgE. Previous research had suggested that GlgE might be essential for the growth of TB bacteria. GlgE would also be an excellent drug target because there are no enzymes similar to it in humans or in the bacteria of the human gut.

The GlgE research revealed a previously unknown enzymatic pathway by which TB bacteria convert the sugar trehalose (consisting of two glucose molecules) into longer sugar molecules known as alpha glucans – building blocks that are essential for maintaining bacterial structure and for making new microbes through cell division. GlgE was the third of four enzymes involved in this pathway leading to alpha glucans molecules.

Sure enough, when the researchers inhibited GlgE, the bacteria underwent "suicidal self-poisoning": a sugar called maltose 1-phosphate accumulated to toxic levels that damaged bacterial DNA, causing the death of TB bacteria grown in Petri dishes as well as in infected mice.

"We were amazed when we knocked out GlgE that we saw this DNA damage response," says Dr. Jacobs. "That's usually a very effective way to kill bacteria, when you start damaging the DNA."

The researchers discovered a second way of killing TB after observing a crucial connection between their novel alpha glucan pathway and a second pathway that also synthesizes alpha glucans.

When the researchers knocked out one of the other enzymes in their novel pathway, the pathway's shutdown didn't kill the bacteria; similarly, inactivating an enzyme called Rv3032 in the second alpha glucan pathway failed to kill the microbes. But inactivating both of those enzymes caused what the researchers term synthetic lethality: two inactivations that separately were nonlethal but together cause bacterial death.

"The bacteria that cause TB need to synthesize alpha glucans," notes Dr. Jacobs. "And from the bacterial point of view, you can't knock out both of these alpha glucan pathways simultaneously or you're dead. So if we were to make drugs against GlgE and Rv3032, the combination would be extremely potent. And since TB bacteria need both of those alpha glucan pathways to live, it's very unlikely that this combination therapy would leave behind surviving bacteria that could develop into resistant strains."

Dr. Jacobs adds that findings from this study could also enhance treatment of diseases caused by other species of mycobacteria. Leprosy, for example, which still occurs in the U.S. and other countries, is caused by a mycobacterium related to TB. Treating leprosy now involves using several different drugs, some of which are also used to treat tuberculosis.

The group's paper, "Self-Poisoning of Mycobacterium tuberculosis by targeting GlgE in an a-glucan pathway," appears in the March 21 online edition of Nature Chemical Biology. In addition to Dr. Jacobs, other Einstein researchers involved in the study were Rainer Kalscheuer, Ph.D., Brian Weinrick, Ph.D., and Karolin E. Biermann, M.S. Other researchers include Karl Syson and Stephen Bornemann, John Innes Centre; Zhen Liu and James C. Sacchettini, Texas A&M University; and Usha Veeraraghavan and Gurdyal Besra; University of Birmingham in the United Kingdom.

Albert Einstein College of Medicine has filed a patent application on the discoveries described in the paper.

Gene is linked to lung cancer development in never-smokers

Researchers say that about 1/3 of never-smokers have this uncommon gene variant

ROCHESTER, Minn. -- A five-center collaborative study that scanned the genomes of thousands of "never smokers" diagnosed with lung cancer as well as healthy never smokers has found a gene they say could be responsible for a significant number of those cancers.

In the March 22 on line issue of Lancet Oncology, the researchers reported that about 30 percent of patients who never smoked and who developed lung cancer had the same uncommon variant, or allele, residing in a gene known as GPC5. The research was co-led by scientists at the Mayo Clinic campus in Minnesota, Harvard University, University of California at Los Angeles (UCLA), and MD Anderson Cancer Center. Researchers found in laboratory studies that this allele leads to greatly reduced GPC5 expression, compared to normal lung tissue. The finding suggests that the gene has an important tumor suppressor-like function and that insufficient function can promote lung cancer development.

"This is the first gene that has been found that is specifically associated with lung cancer in people who have never smoked," says the study's lead investigator, Ping Yang, M.D., Ph.D., Mayo Clinic genetic epidemiologist.

"What's more, our findings suggest GPC5 may be a critical gene in lung cancer development and genetic variations of this gene may significantly contribute to increased risk of lung cancer," she says. "This is very exciting."

The research teams scanned and analyzed the genomes of 2,272 participants who have never smoked, nearly 900 of whom were lung cancer patients. It took researchers 12 years to identify and enroll these study participants.

"It has been very hard to do this research because never smokers have been mingled with smokers in past studies, and what usually pops up are genes related to nicotine dependence," Dr. Yang says.

"Findings from this study concern pure lung cancer that is not caused by smoking, and it gives us some wonderful new avenues to explore."

Little is known about the GPC5 gene, except that it can be over-expressed in multiple sclerosis, and that alterations in the genome where GPC5 is located are a common event in a wide variety of human tumors. "It may be that GPC5 holds different roles depending on the tissue type during various disease development and progression," Dr. Yang says.

A never smoker is defined as a person who has smoked fewer than 100 cigarettes in his or her lifetime, and that describes 15 percent of men and 53 percent of women who develop lung cancer -- accounting for 25 percent of all lung cancers worldwide, according to Dr. Yang. In the Western countries, between 10 and 15 percent of lung cancers occur among never smokers, but in Asian countries, 30 to 40 percent of lung cancers

are never smokers, she says. "Our suspicion all along is that this is a distinct disease, and that is why we undertook this study," Dr. Yang says.

The research took two years and involved four steps. In the first step, conducted at Mayo Clinic, a genome-wide association study (GWAS) was performed on 377 never smokers with lung cancer, matched with 377 participants without lung cancer, the "control" population. This was the first GWAS ever conducted solely among never smokers, and it involved scanning the entire genome of every participant, looking for differences among 300,000 markers or so-called single-nucleotide polymorphisms (SNPs). The scan looks at everything -- inside and outside genes, coding and noncoding regions, Dr. Yang says. They found 44 "hits" -- hinting 44 areas on the genome that were substantially different between the lung cancer patients and healthy control population.

Then, to rigorously validate their findings in other populations, researchers launched stage 2. That involved using data from two more GWAS scans in independent populations -- 328 never smoker lung cancer patients and 407 controls at MD Anderson Cancer Center, and 92 never smoker lung cancer patients and 161 controls at Harvard University. From this, the search was narrowed to just two hits. Both of these hits were adjacent to each other on the same gene, which the researchers then identified as a variant of GPC5.

In the third stage of the study, the researchers used a different method to perform genotyping from the method used in stages 1 and 2 to look at the difference between 91 never smoker lung cancer patients and 439 controls at UCLA. "We confirmed the variant-lung cancer association again," Dr. Yang says.

The final stage of the study involved understanding the function of the gene. "We had to understand whether these hits really represented the functional aspect of the gene, so we tested expression level of GPC5 and found it was significantly reduced," Dr. Yang says. They found that the GPC5 transcription level was twofold lower in adenocarcinoma compared to normal lung tissue. "Interestingly, this reduced transcript expression level was not found in lung carcinoid tumors," Dr. Yang says.

Then the researchers looked to see if this reduced expression led to tumor development, which it did in laboratory culture. "If reduction of expression of this gene leads to development of lung cancer, it suggests that this gene is normally a tumor suppressor," Dr. Yang says. "We believe it helps control the cell proliferation and division, but we need to prove its function in animal models."

They calculated that about one-third of never smoker lung cancer patients in this study had the same variation of the underperforming GPC5 gene. "We hypothesize that this is an important cancer trigger in these patients, and that something else is going on in the remaining two-thirds of never smokers," she says.

"We don't know what that is, but we now have 42 other hits to explore," Dr. Yang says.

The study was funded by the National Institutes of Health and the Mayo Foundation. The authors declared no conflicts of interest.