

Nature's laws may vary across the Universe

One of the laws of nature may vary across the Universe, according to a study published today in the journal *Physical Review Letters*.

PhysOrg.com - One of the most cherished principles in science - the constancy of physics - may not be true, according to research carried out at the University of New South Wales (UNSW), Swinburne University of Technology and the University of Cambridge.

The study found that one of the four known fundamental forces, electromagnetism - measured by the so-called fine-structure constant and denoted by the symbol 'alpha' - seems to vary across the Universe.

The first hints that alpha might not be constant came a decade ago when Professor John Webb, Professor Victor Flambaum, and other colleagues at UNSW and elsewhere, analysed observations from the Keck Observatory, in Hawaii. Those observations were restricted to one broad area in the sky.

How a galaxy imprints a "barcode" of metallic absorption lines onto the spectrum of a background quasar. We read this barcode after recording the quasar spectrum with telescopes on the Earth. The barcode encodes the laws of physics in the distant, absorbing galaxy, so we can tell whether the laws of physics change throughout the universe, or really stay constant like is currently assumed. IMAGE CREDITS: Quasar spectrum: Michael Murphy, Swinburne University of Technology; Hubble Ultra Deep Field: NASA, ESA, S. Beckwith (STScI) and the HUDF Team.

However, now Webb and colleagues (PhD graduate Dr Julian King, PhD student Matthew Bainbridge and Professor Victor Flambaum at UNSW; Dr Michael Murphy at Swinburne University of Technology, and Professor Bob Carswell from Cambridge University) have doubled the number of observations and measured the value of alpha in about 300 distant galaxies, all at huge distances from Earth, and over a much wider area of the sky. The new observations were obtained using the European Southern Observatory's 'Very Large Telescope' in Chile.

"The results astonished us," said Professor Webb. "In one direction - from our location in the Universe - alpha gets gradually weaker, yet in the opposite direction it gets gradually stronger."

Illustration of the direction of the dipolar axes from our study on the sky, in equatorial coordinates. The green region corresponds to the direction of the dipole derived only from Keck telescope quasar spectra. The blue region shows the dipole direction from the VLT spectra alone. The red region shows the dipole region from the combined dataset from both telescopes. The light grey ring represents the Milky Way, as projected onto the equatorial coordinate frame, with the Galactic centre shown as a bulge. IMAGE CREDIT: Appears in published version of the paper, <http://prl.aps.org/abstract/PRL/v107/i19/e191101>

"The discovery, if confirmed, has profound implications for our understanding of space and time and violates one of the fundamental principles underlying Einstein's General Relativity theory," Dr King added.

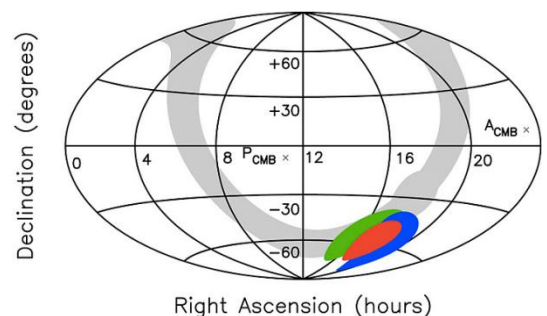
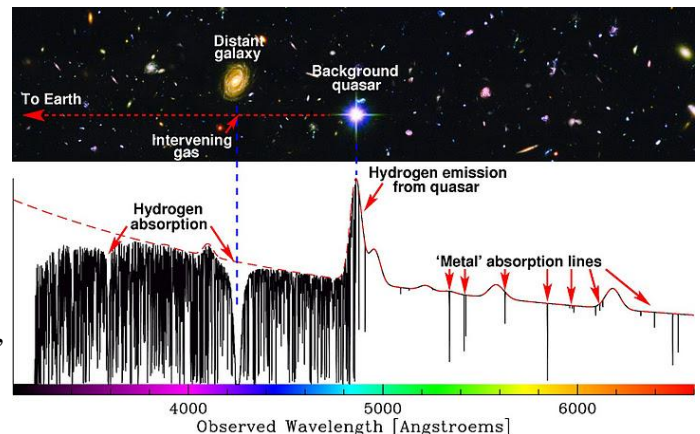
"Such violations are actually expected in some more modern 'Theories of Everything' that try to unify all the known fundamental forces," said Professor Flambaum. "The smooth continuous change in alpha may also imply the Universe is much larger than our observable part of it, possibly infinite."

"Another currently popular idea is that many universes exist, each having its own set of physical laws," Dr Murphy said. "Even a slight change in the laws of Nature means they weren't 'set in stone' when our Universe was born. The laws of Nature you see may depend on your 'space-time address' - when and where you happen to live in the Universe."

Professor Webb said these new findings also offer a very natural explanation for a question that puzzled scientists for decades: why do the laws of physics seem to be so finely-tuned for the existence of life?

"The answer may be that other regions of the Universe are not quite so favourable for life as we know it, and that the laws of physics we measure in our part of the Universe are merely 'local by-laws', in which case it is no particular surprise to find life here," he said.

More information: A pre-print version is available at arXiv:1008.3907. <http://www.astronomy.aphy/res.html>
Provided by Swinburne University of Technology



Fecal microbiota transplants effective treatment for C. difficile, Inflammatory Bowel Disease

Long-term follow-up of potentially life-saving procedure provides further evidence of efficacy

Washington, DC - Growing evidence for the effectiveness of fecal microbiota transplants as a treatment for patients with recurrent bouts of Clostridium difficile (C.difficile) associated diarrhea is presented in three studies - including a long-term follow-up of colonoscopic fecal microbiota transplant (FMT) for recurrent C. difficile Infection that included 77 patients from five different states - unveiled today at the American College of Gastroenterology's (ACG) 76th Annual Scientific meeting in Washington, DC.

In a fourth study, investigators from the Centre for Digestive Diseases in Australia explored fecal bacterial transplantation as a treatment for Inflammatory Bowel Disease. While this is a new area of research, results of this study show success in treating IBD when the fecal transplant is done recurrently.

The first study, "Long-term Follow-up of Colonoscopic Fecal Microbiota Transplant (FMT) for Recurrent C. difficile Infection (RCDI)," included 77 patients from five different states (RI, NY, OK, CA, WA) who previously had a colonoscopic fecal microbiota transplant at least three months ago for recurrent C. difficile infection, and found that FMT was successful in 70 out of 77 patients (91 percent) who were on average elderly, debilitated and had undergone multiple failed treatments, including antibiotic and probiotic therapies. Additionally, in six of the remaining seven patients, a single two-week course of vancomycin or a two-week vancomycin course plus one further FMT resulted in cure (98 percent).

"Many of these patients we followed up with had been ill for a long time, but once they underwent the fecal microbiota transplant their response to the treatment was quick and their symptoms improved on average in about six days," said investigator Mark H. Mellow, MD, FACG, of INTERGRIS Baptist Medical Center in Oklahoma. The average duration of illness for these patients was 11 months, but after the procedure patients continued to improve and - without subsequent antibiotic treatment - did not have a recurrence of C. difficile infection during follow-up (on average, 17 months), according to Dr. Mellow and his team of co-investigators which included a leading pioneer of fecal microbiota transplantation, Lawrence J. Brandt, MD, MACG, of the Albert Einstein College of Medicine in New York.

Results from a meta-analysis by researchers at the University of Toledo Medical Center were also unveiled today, providing further evidence of the effectiveness of fecal microbiota transplantation.

"Fecal Bacteriotherapy Works for Clostridium difficile Infection - A Meta-Analysis," reviewed the cases of 148 patients who had received fecal transplants for C. difficile infection. Follow-up ranged from 10 days to 62 months after the transplant, with an average follow-up of 1 year. Fecal transplant had an overall success rate of 85.4 percent, according to researchers, who also concluded that the procedure was a safe and effective treatment option for C. difficile infection.

Clostridium difficile is a bacterium that causes infection leading to diarrhea and is most often related to antibiotic use during medical treatment. A major cause of morbidity and increasing health care costs among hospitalized patients, C. difficile infections have dramatically increased in recent years, with 500,000 cases in the United States annually and approximately 15,000 deaths each year, according to the U.S. Centers for Disease Control & Prevention. Up to 25 percent of patients will have a recurrence of C. difficile infection, and a proportion will be refractory to antibiotics. C. difficile is especially dangerous for patients with weakened immune systems such as the elderly and those with Inflammatory Bowel Disease (IBD). Therapies for this difficult to treat subpopulation include antibiotics, probiotics, toxin-binding medications, active vaccination, intravenous immunoglobulin, and fecal microbiota transplant, for which the evidence has been mounting as an effective rescue for recurrent and refractory cases of C. difficile associated diarrhea.

"While the concept of fecal transplantation may sound unpleasant to some, patient acceptance of this treatment is growing, especially when they have been suffering for months with recurrent C. difficile," said Dr. Mellow. "When we asked patients in our study about their choice of treatment if their infection recurred, 53 percent said fecal transplant would be their first choice for treatment."

In a related study also unveiled today, "Clostridium Difficile Infection in Ulcerative Colitis: Increased Risk of Colectomy and Postoperative Infectious Complications," researchers from the University of Calgary found that patients with ulcerative colitis who were diagnosed with C. difficile were significantly less likely to respond to medical treatment and as a result require a colectomy when they diagnosed with C. difficile in the hospital or within 90 days of admission. In addition, patients with ulcerative colitis who had concomitant C. difficile, preoperatively were at a higher risk of infectious complications following a colectomy.

Researchers Find Fecal Microbiota Transplantation Effective For Treatment of IBD

With the growing success of fecal transplantation for C.Difficile, researchers have started to explore the effectiveness of this procedure for other serious conditions, such as Inflammatory Bowel Disease (IBD). A second study, "Reversal of Inflammatory Bowel Disease (IBD) with Recurrent Fecal Microbiota Transplants (FMT)," reports successful treatment of severe mixed IBD using recurrent fecal microbiota transplants in three patient cases.

In Case 1, a 19-year old female with an 11-year history of severe IBD and who presented with worsening symptoms including bloody diarrhea and inflamed, ulcerated mucosa, and was considering a colectomy, experienced symptom improvement within several days after receiving FMT. She underwent FMT initially via colonoscopy in July 2009 then by seven daily rectal FMT and 26 weekly FMT's. Follow-up colonoscopy revealed no gross inflammation or edema, with the patient remaining clinically well.

In Case 2, a 23- year old male with a five-year history of steroid and anti-TNF α refractory ulcerative colitis presented with bloody diarrhea more than 20 times per day, anal fissures, severe abdominal pain and joint pain. Pre-FMT colonoscopy - showed severe disease of the left colon with marked cecal inflammation. He underwent daily rectal FMT for the first month, followed by infusions of lessening frequency until he reached 1 FMT/6 weeks. He reported resolution of bleeding 1-2 weeks post-FMT, and formed stool at 1 month post-FMT, resumed work, study activities and regained weight. Colonoscopy at one year showed no histological inflammation but occasional pseudopolyps in the cecum and ascending colon.

In Case 3, a 57-year old female with a nine- year history of 5-ASA antibiotics, probiotics and immunosuppressant refractory ulcerative proctitis in spite of treatment. After training in our clinic, she performed 69, initially daily, then weekly rectal FMT with virtually immediate resolution of diarrhea, bleeding and mucus. Follow-up colonoscopy showed no visible or histological inflammation and she has remained off all therapy for the last four years.

FMT may act as an antagonist to etiological infective agent(s) and aid in re-establishing depleted bacterial species, thereby reversing IBD, according to researchers from the Centre for Digestive Diseases in Australia.

Commenting on the cases of FMT in IBD, lead researcher Thomas Borody, MD, PhD, FACP, said, "the rapid response of FMT and lack of adverse effects make FMT a viable option for treatment-refractory patients and is certainly an added option for those facing colectomy."

http://www.eurekalert.org/pub_releases/2011-10/uov-ffw103111.php

Fighting fire with fire: 'Vampire' bacteria has potential as living antibiotic
A vampire-like bacteria that leeches onto specific other bacteria - including certain human pathogens - has the potential to serve as a living antibiotic for a range of infectious diseases, a new study indicates.

The bacterium, *Micavibrio aeruginosavorus*, was discovered to inhabit wastewater nearly 30 years ago, but has not been extensively studied because it is difficult to culture and investigate using traditional microbiology techniques. However, biologists in the University of Virginia's College of Arts & Sciences, Martin Wu and graduate student Zhang Wang, have decoded its genome and are learning "how it makes its living," Wu said.

The bacterium "makes its living" by seeking out prey - certain other bacteria - and then attaching itself to its victim's cell wall and essentially sucking out nutrients. Unlike most other bacteria, which draw nutrients from their surroundings, *M. aeruginosavorus* can survive and propagate only by drawing its nutrition from specific prey bacteria. This kills the prey - making it a potentially powerful agent for destroying pathogens.

One bacterium it targets is *Pseudomonas aeruginosavorus*, which is a chief cause of serious lung infections in cystic fibrosis patients.

"Pathologists may eventually be able to use this bacterium to fight fire with fire, so to speak, as a bacterium that will aggressively hunt for and attack certain other bacteria that are extremely harmful to humans," Wu said.

His study, detailing the DNA sequence of *M. aeruginosavorus*, is published online in the journal BMC Genomics [link: <http://www.biomedcentral.com/1471-2164/12/453>]. It provides new insights to the predatory lifestyle of the bacterium and a better understanding of the evolution of bacterial predation in general.

"We used cutting-edge genomic technology in our lab to decode this bacterium's genome," Wu said. "We are particularly interested in the molecular mechanisms that allow it to hunt for and attack prey. This kind of investigation would have been extremely difficult and expensive to do only a few years ago."

He noted that overuse of traditional antibiotics, which work by either inhibiting bacteria propagation or interfering with cell wall formation, are creating so-called "super bugs" that have developed resistances to treatment strategies. He suggests that new approaches are needed for attacking pathogens without building up their resistance. Additionally, because *M. aeruginosavorus* is so selective a feeder, it is harmless to the thousands of beneficial bacteria that dwell in the general environment and in the human body.

"It is possible that a living antibiotic such as *M. aeruginosavorus* - because it so specifically targets certain pathogens - could potentially reduce our dependence on traditional antibiotics and help mitigate the drug-resistance problem we are now facing," Wu said. Another benefit of the bacterium is its ability to swim through viscous fluids, such as mucus. *P. aeruginosavorus*, the bacterium that colonizes the lungs of cystic fibrosis patients, creates a glue-like biofilm, enhancing its resistance to traditional antibiotics. Wu noted that the living cells of *M. aeruginosavorus* can swim through mucus and biofilm and attack *P. aeruginosavorus*.

M. aeruginosavorus also might have industrial uses, such as reducing bacteria that form biofilms in piping, and for medical devices, such as implants that are susceptible to the formation of biofilms.

Wu said *M. aeruginosavorus* requires further study for a more thorough understanding of its gene functions. He said genetic engineering would be required to tailor the predatory attributes of the bacterium to specific uses in the treatment of disease. "We have a map now to work with, and we will see where it leads," he said.

Wu and Wang's co-author is Daniel E. Kadouri, a researcher at the New Jersey Dental School. Kadouri is interested in M. aeruginosavorus as an agent for fighting oral biofilms, such as plaque.

http://www.eurekalert.org/pub_releases/2011-10/acog-mac102711.php

Moderate alcohol consumption is associated with small intestinal bacterial overgrowth

Just one drink per day may be cause of GI woes like bloating, gas, abdominal pain, diarrhea

Washington, DC - Just one drink per day for women - two for men - could lead to small intestinal bacterial overgrowth (SIBO) and subsequently cause gastrointestinal symptoms like bloating, gas, abdominal pain, constipation and diarrhea, according to the results of a new study unveiled today at the American College of Gastroenterology's (ACG) 76th Annual Scientific meeting in Washington, DC.

The retrospective review, "Moderate Alcohol Consumption is Associated with Small Intestinal Bacterial Overgrowth," looked at the charts of 198 patients who underwent lactulose hydrogen breath testing (LHBT) to determine the presence of SIBO, and found that any current alcohol consumption was significantly associated with the presence of SIBO- and neither smoking nor use of heartburn drugs called PPIs was associated with an increased risk of SIBO.

Small intestinal bacterial overgrowth is a condition where abnormally large numbers of bacteria grow in the small intestine. Normally the small intestine contains a relatively low number of bacteria in contrast to the large intestine, which should contain a larger number of bacteria. In patients with SIBO, the abnormally large numbers of bacteria in the small intestine use for their growth many of the nutrients that would otherwise be absorbed. As a result, a person with small bowel bacterial overgrowth may not absorb enough nutrients and become malnourished. In addition, the breakdown of nutrients by the bacteria in the small intestines can produce gas as well as lead to a change in bowel habits.

While previous studies have focused on alcoholics, who were found to have high rates of SIBO, this study by Scott Gabbard, MD and colleagues at the Dartmouth-Hitchcock Medical Center and the Mayo Clinic, is one of the first to look at the relationship between moderate alcohol consumption and SIBO. Moderate alcohol consumption means no more than 1 drink per day for women and 2 drinks per day for men, with twelve ounces of regular beer, 5 ounces of wine, or 1-½ ounces of 80-proof distilled spirits counting as one drink, according to the USDA dietary guidelines.

An overwhelming majority (95 percent) of the 198 patients in the study drank a moderate amount of alcohol, sometimes less than 1 drink per day, said Dr. Gabbard, who also indicated that only four of the patients drank more alcohol - a finding he noted indicates that consumption of even the slightest amount of alcohol could have an impact on gut health.

"These findings are significant because we now know that any bit of alcohol consumption - not just the amount consumed by alcoholics - is a strong predictor of a positive lactulose hydrogen breath testing and small intestinal bacterial overgrowth," he said. "While typical treatment for SIBO has been antibiotics, probiotics or a combination of the two, the question now becomes what is the exact association between moderate alcohol consumption and SIBO and whether alcohol cessation can be used as a treatment for this potentially harmful condition."

http://www.eurekalert.org/pub_releases/2011-10/acog-pwp102711.php

Physicians who play Mozart while performing colonoscopy may improve adenoma detection rate

New study highlights importance of adenoma detection rate as quality indicator for colonoscopy

Washington, DC - Physicians who listen to Mozart while performing colonoscopy may increase their detection rates of precancerous polyps, according to the results of a new study unveiled today at the American College of Gastroenterology's (ACG) 76th Annual Scientific meeting in Washington, DC.

The study, "The 'Mozart Effect' and Adenoma Detection," by Catherine Noelle O'Shea, DO and David Wolf, MD, of the University of Texas Health Science Center at Houston, found adenoma detection rate - the proportion of patients undergoing screening colonoscopy in whom an adenomatous polyp is found and an important measure of a high quality endoscopic exam - increased from baseline values with music compared to without for two endoscopists whose baseline adenoma detection rates were calculated over a one-year period prior to the start of the study. The "Mozart Effect" refers to a set of research results that found listening to Mozart's music may result in significant short-term improvement in spatial temporal reasoning. Researchers used this previous theory to determine whether or not listening to Mozart while performing a colonoscopy had any impact on an endoscopist's adenoma detection rate.

In this randomized controlled trial, two endoscopists each with experience completing at least 1000 colonoscopies performed screening colonoscopies randomly assigned to music - where Mozart was played - or no music. Each endoscopist was unblinded to music exposure. Adenoma detection rates from this study were than calculated and compared to the baseline rates. "Both endoscopists had higher adenoma detection rates listening to music when compared with their baseline rates," said lead researcher Dr. O'Shea.

Endoscopist #1, who was blinded to outcome, had an adenoma detection rate of 66.7 percent listening to Mozart and 30.4 percent without the music. Endoscopist #2, who was unblinded to the outcome, had an adenoma detection rate of 36.7 percent with Mozart and 40.5 percent without the music. Baseline detection rates were 21.25 percent (Endoscopist #1) and 27.16 percent (Endoscopist #2).

Adenomas are a type of colon polyp that is considered a precursor for invasive colorectal cancer (CRC), which is the third most common cancer diagnosed in men and women in the United States and the second leading cause of cancer death when both sexes are combined. According to the American Cancer Society, 102,900 new cases of colon cancer (49,470 in men and 53,430 in women) were diagnosed in the United States in 2010.

"Adenoma detection rate is linked to a reduction in colorectal cancer incidence so it is an important quality indicator for colonoscopy," said Dr. O'Shea. "Anything we can do get those rates up has the potential to save lives. While this is a small study, the results highlight how thinking outside the box - in this case using Mozart - to improve adenoma detection rates can potentially prove valuable to physicians and patients."

A study published last May in The New England Journal of Medicine found that adenoma detection rate is an independent predictor of the risk of interval colorectal cancer after screening colonoscopy - data from the study showed that when endoscopists frequently find polyps during their exams, there are fewer interval cancers diagnosed between tests. When that rate falls below 20 percent, the risk of colorectal cancer being diagnosed within the next five years goes up significantly. When the rate was below 11 percent, the risk of an interval cancer was more than 10 times higher than when adenomas were found more than 20 percent of the time.

When detected early, polyps can be removed during a colonoscopy exam, preventing the development of colorectal cancer. This ability to prevent colorectal cancer through polyp removal is the cornerstone of the American College of Gastroenterology's 2009 screening guideline which recommends colonoscopy as a "preferred" colorectal cancer prevention strategy. A tremendous body of evidence shows that clearing the colon of polyps, including small polyps, significantly reduces colorectal cancer mortality. When detected in its earliest and most treatable stage, the survival rates for colorectal cancer exceed 90 percent.

<http://nyti.ms/sAhGh5>

Really? The Claim: For a More Restful Nap, Avoid Caffeine

THE FACTS *Late November is the start of the busiest travel season of the year, when millions of drivers hit the road for long-distance treks. Many will be sleep-deprived and looking to pull over for a nap or a dose of caffeine.*

By ANAHAD O'CONNOR

But the best idea may be to combine the two, and not in the order one might think. Ordinarily, sleep experts advise steering clear of coffee and other stimulants before resting, since caffeine disrupts sleep. As a result, studies on drowsy drivers have generally compared the restorative benefits of pulling over and napping versus pulling over for a cup of caffeine. Researchers have found that a 15- to 30-minute nap increases alertness and driving performance, but most studies show that drinking caffeine is a slightly superior strategy.

In a series of studies, however, sleep researchers in England found that drinking a cup of coffee and then immediately taking a 15-minute nap was even more effective. The researchers tested sleep-deprived subjects in driving simulators and found that a "caffeine nap" improved driving performance and reduced sleepiness better than other commonly employed techniques, including cold air, a short nap, a break with no nap or 200 milligrams of caffeine, roughly the amount in a 10-ounce cup of strong brewed coffee.

This method is believed to work because the short power nap helps clear the brain of the sleep-inducing compound adenosine. Caffeine, meanwhile, takes about 20 minutes to have its physiological effect - kicking in just as the napper is awakening.

THE BOTTOM LINE A cup of coffee followed by a 15-minute nap may be more restorative than either one alone.

<http://news.discovery.com/human/black-licorice-111031.html>

Beware Black Licorice

With wrapped treats aplenty this Halloween, there's one candy to embrace in moderation.

By Marianne English | Sun Oct 30, 2011 04:15 PM ET

The U.S. Food and Drug Administration warns that consuming too much black licorice could lead to heart arrhythmias, especially in the 40-and-over crowd.

Here's why: A main ingredient in black licorice root, glycyrrhizin, can lower potassium levels in a person's body, which can have negative effects on the heart. The FDA sets limitations on how much glycyrrhizin can be used in food products, but people can still take in more of the ingredient through eating multiple servings.

Health officials say people 40 and older should avoid consuming more than 2 ounces of the treat for consecutive days. One case study suggests a patient experienced pulmonary edema, a side effect of heart failure, from binging on black licorice.

For most healthy people, an irregular heartbeat usually doesn't cause health problems, but the condition can be harmful for some. Signs of a heart arrhythmia include a racing heartbeat, chest pain, shortness of breath and a slow heartbeat, among others, according to the Mayo Clinic. Most cases are resolved after a patient quits eating the black candy. But for black licorice lovers of any age, be careful about eating too much of the stuff, recommends the FDA.

If you're unsure about whether a given candy or food contains glycyrrhizin, check the nutrition label to see if terms such as "licorice extract" or "licorice root extract" are listed among the ingredients, says Hershey's, the manufacturer of popular licorice products in the United States such as Twizzlers and Good & Plenty.

Licorice root may also be present in certain dietary supplements, too. But some products offer licorice with the glycyrrhizin removed. The government also discourages pregnant women from taking any amount of licorice because of the root's potential ability to affect the health of moms and babies. In one experiment, licorice consumption was linked to early birth in some women.

<http://medicalxpress.com/news/2011-10-short-significantly-precancerous-polyps.html>

Short training course significantly improves detection of precancerous polyps

Just two extra hours of focused training significantly increased the ability of physicians to find potentially precancerous polyps, known as adenomas, in the colon, according to researchers at Mayo Clinic in Florida.

These findings suggest that new methods to educate endoscopists, the physicians who examine the colon, could increase colorectal cancer detection rates and potentially reduce cancer deaths. Results of the study were presented at the annual meeting of the American College of Gastroenterology in Washington, D.C.

"Colorectal cancer screening, which has been proven to save many lives, is steadily improving due to better detection of precancerous polyps, but this study shows us that more can be done," says first author Susan Coe, M.D., who is in her third year of training as an endoscopist.

The prototype training course was developed by physicians at Mayo Clinic in Florida and evaluated in a randomized clinical study at the institution. Endoscopists at Mayo Clinic in Florida already have an adenoma detection rate that is higher than the national average. But the extra training examined in this study significantly increased that rate. National guidelines suggest that, on average, physicians should be detecting precancerous polyps in 25 percent of men and women who are examined. The detection rate at Mayo Clinic before training was 36 percent, and after training increased to 47 percent.

"Like other screening tests, there is always room for improvement, and that is particularly true in colonoscopy in the detection of very small or hard-to-see polyps," says the study's senior investigator, Michael Wallace, M.D., M.P.H., chief of the Division of Gastroenterology and Hepatology at Mayo Clinic in Florida. "In this study we were able to develop new educational methods based on the latest information on characteristics of challenging polyps that are often difficult to see."

The researchers established a clinical trial, the Endoscopic Quality Improve Program (EQUIP), to test the two one-hour training sessions they developed. To create that program, the researchers surveyed the medical literature, as well as videos and detection techniques, to find certain techniques that appear to improve polyp

detection rates. Those techniques included cleaning the colon adequately, and looking behind the folds in the colon to find hard-to-detect polyps, such as those that are flat or serrated.

The study was conducted in two phases. In the first phase, 15 Mayo Clinic endoscopists completed 1,200 colonoscopies, and their adenoma detection rate was calculated. Then a group of endoscopists were randomly selected to undergo the training, and the second phase measured the effect of this training. Those who did not receive the training sessions had a detection rate of 35 percent in the second phase of the study, compared to 47 percent in physicians who attended the courses. That new rate was "one of the highest ever reported for a large group of endoscopists," Dr. Wallace says.

"It isn't that endoscopists aren't being continually trained. They are, through continuing medical education courses and quality improvement initiatives," Dr. Coe says. "The issue is that these training methods may not be focusing enough attention on the best methods to find adenomas."

The researchers plan to validate their findings in a widespread clinical trial that includes the community physicians who perform the majority of colonoscopies. "The most rigorous way to prove that something works is a randomized controlled trial comparing the current standard of care with the extra educational efforts, as was done in this trial," says Dr. Wallace. "While we all speculated that the education would help, now we know that it does, and we can use that information to make even further improvements and apply this more broadly."

Provided by Mayo Clinic

<http://www.scientificamerican.com/article.cfm?id=sensomics-chocolate-smell>

The Sweet Smell of Chocolate: Sweat, Cabbage and Beef

The new discipline of "sensomics" is helping to find ways to make chocolate even tastier

By Carrie Arnold | Monday, October 31, 2011 | 2

Chocolate may be the most sought-after treat among trick-or-treaters on Halloween, with little hands grasping for all of the milk- and dark-chocolate morsels they can collect, but the details of its taste and aroma profiles have long eluded scientists.

And new science is revealing why cocoa's potent sensual properties have been so difficult to pin down. A recent analysis found that the individual aroma molecules in roasted cacao beans (the primary ingredient of chocolate) can smell of everything from cooked cabbage to human sweat to raw beef fat. Together, more than 600 of these flavor compounds melt together in just the right combination to yield the taste and scent of what we all call chocolate, according to Peter Schieberle, a food chemist at Munich Technical University and director of the German Research Center for Food Chemistry, who presented the data at this year's meeting of the American Chemical Society in Denver.

Most of the molecules that comprise a food's aroma are volatile, which means they transform into gases easily at room temperature. These volatile compounds are inhaled along with the air we breathe, bringing them into contact with the 900-plus odorant receptors in the upper half of the nostril. In the early 1990s scientists Linda Buck and Richard Axel began the work that would show each odorant receptor recognized one particular compound and was linked to a specific olfactory neuron in the nostril. As a volatile aroma compound latches onto an odorant receptor, it triggers the firing of the olfactory neuron (Buck and Axel won the 2004 Nobel Prize in Physiology or Medicine for their discovery). Complex aromas form when multiple volatile compounds trigger their respective olfactory neurons at the same time. The brain identifies flavor by measuring how frequently the different neurons fire.

"By the time you put four chemicals together, your brain can no longer separate them into components. It forms a new, unified perception that you can't recognize as any of those individual aromas," says Gary Reineccius, a food scientist at the University of Minnesota.

Processed foods such as chocolate, beer and tea contain thousands of aroma compounds. This multiplicity of molecules creates a mosaic of odor in the brain as each individual molecule contributes a hint of scent to the final flavor. Just as our brains can often assemble a whole picture from seeing just a sketch of an image, Schieberle and colleagues found that humans can recognize chocolate aroma using only 25 of its 600-plus volatile compounds. Of these, many are also found in much less appetizing items, including cooked cabbage, raw beef fat and human sweat, which are in turn also composed of many different volatile compounds.

Even so, not one of these 25 key compounds can be pegged as a "chocolate" aroma. "The mixture smells completely different from the individual constituents," Schieberle says. "At the moment, there is no way to predict how the final mixture will smell."

Schieberle calls the study of individual aroma and flavor molecules "sensomics," which sifts through the countless potential aroma compounds for those molecules of particular importance to human taste and smell. Schieberle's work has identified which aroma compounds from roasted cacao beans could bind to odor

receptors in humans. None of them, it turned out, smell anything at all like the sweet, rich scent we identify as chocolate.

To figure out exactly which molecules contributed to chocolate aroma, Schieberle and colleagues had to pick apart chocolate aroma one molecule at a time. First, the researchers identified those volatile compounds that would react with human odor receptors and were present at high enough levels to register in the brain, which yielded 25 different molecules. These molecules included 2- and 3-methylbutanoic acids (both produce a sweaty, rancid odor), dimethyl trisulfide (cooked cabbage) and 2-ethyl-3,5-dimethylpyrazine (potato chips). Then, they blended these rather un-chocolatey aroma molecules in different combinations and asked human study subjects to smell them. The blend that contained all of the 25 volatile aroma molecules could reliably fool the nose and brain into thinking it had smelled chocolate. These 25 compounds are what Schieberle refers to as chocolate's chemical signature - those volatile compounds in chocolate that trigger human olfactory nerves in just the right combination "causing a signal in the brain to say 'this is chocolate,'" Schieberle says.

What we think of as "chocolate" smell is due in large part to the way in which the food is made - a process that includes both fermentation and roasting. Foods that are processed by fermentation, roasting or grilling such as wine, coffee and steak, respectively, generally contain the most aroma molecules. It is this process's conversion of otherwise odorless compounds into volatile aroma-bearing ones that helps explain this type of food's popularity. Natural, raw foods like fruits and vegetables also have an appealing aroma and taste, although their flavor profile is much simpler and usually dominated by one or two major molecules.

"That chemical really creates that flavor, and everything else kind of smoothes it and makes it pleasant," Reineccius says of these less complex foods. The combination of volatile aroma compounds as well as the sugars and salts that we taste during chewing combine to create flavor. "Some of our simpler flavors are strawberry and raspberry because they're just what nature happened to provide to keep itself living." The replication of these flavors by food chemists has previously been a process of trial and error.

The goal of his work, Schieberle says, is not to develop artificial chocolate flavorings. Rather, his goal is to find ways to tweak the cacao bean fermentation and roasting process to develop even better tasting chocolates. A recent discovery in his lab, made earlier this year, has taken a small step in this direction. Cacao beans processed in the so-called Dutch style, which adds alkali salt during roasting, have a milder, more pleasant flavor. After deconstructing the molecular makeup of this form of chocolate, the researchers knew that it contained molecules that had a pleasant "mouthfeel." And by adding a tiny bit of glucose to the cacao beans during the Dutch roasting process, Schieberle and colleagues, did not increase the sweetness of the final product, but instead created a more velvety mouthfeel in the final chocolate.

Better understanding chocolate's alluring aroma can also help with tasting technique. Let the chocolate dissolve on your tongue, Schieberle says, so that you can taste the full array of flavor compounds. As the chocolate melts in your mouth and you exhale, some of the volatile molecules will once again pass over your odor receptors, letting you get another whiff before the chocolate melts away.

http://www.eurekalert.org/pub_releases/2011-11/nifp-aoi102611.php

Abnormal oscillation in the brain causes motor deficits in Parkinson's disease
A group has shown that the 'oscillatory' nature of electrical signals in subcortical nuclei, the basal ganglia, causes severe motor deficits in Parkinson's disease

The research group headed by Professor Atsushi Nambu (The National Institute for Physiological Sciences) and Professor Masahiko Takada (Primate Research Institute, Kyoto University) has shown that the 'oscillatory' nature of electrical signals in subcortical nuclei, the basal ganglia, causes severe motor deficits in Parkinson's disease, by disturbing the information flow of motor commands. The group also found that chemical inactivation of the subthalamic nucleus (a structure of the basal ganglia) in parkinsonian monkeys improved the motor impairments by reducing the 'oscillations.' The results of this study were reported in European Journal of Neuroscience, November 2011 issue.

A member of the research group, Assistant Professor Yoshihisa Tachibana, succeeded to record electrical signals in monkey basal ganglia neurons under unanesthetized conditions. The group found that neurons in the parkinsonian basal ganglia showed abnormal 'oscillatory' activity, which was rarely seen in normal subjects. The abnormal rhythm was completely eliminated by systemic administration of a dopamine precursor (L-DOPA), which is clinically used for human parkinsonian patients. The group considered that loss of dopamine induced the 'oscillations' in the basal ganglia and that the following disturbances in information flow of motor commands impaired motor performances.

Abnormal neuronal oscillations were already reported in parkinsonian patients and animal models, but this report has provided the direct evidence that 'oscillations' are associated with motor abnormalities. Moreover, it

was also shown that the injection of a chemical inhibitor, muscimol, into the subthalamic nucleus silenced the oscillatory signals, and eventually reversed parkinsonian motor signs.

Professor Nambu claims, "By investigating the 'oscillatory' nature of electrical signals in the basal ganglia, we can advance our understanding of the pathophysiology of Parkinson's disease. We improved motor deficits by means of infusion of the chemical inhibitor (muscimol) into the subthalamic nucleus to silence the 'oscillatory' signals in the brain structure. This may provide us important clues to developing new treatments for Parkinson's disease."

This study was supported by Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan, the Japan Intractable Diseases Research Foundation and Hori Information Science Promotion Foundation to Y. Tachibana and A. Nambu, and NIH grants (NS-47085 and NS-57236) to H. Kita.

http://www.eurekalert.org/pub_releases/2011-11/foas-ctf110111.php

Catch the fever: It'll help you fight off infection

New research published in the Journal of Leukocyte Biology demonstrates that elevated body temperature plays a vital role on the generation of effective T-cell mediated immune response

Bethesda, MD - With cold and flu season almost here, the next time you're sick, think twice before taking something for your fever. That's because scientists have found more evidence that elevated body temperature helps certain types of immune cells to work better. This research is reported in the November 2011 issue of the Journal of Leukocyte Biology (<https://www.jleukbio.org>).

"An increase in body temperature has been known since ancient times to be associated with infection and inflammation," said Elizabeth A. Repasky, Ph.D., a researcher involved in the work from the Department of Immunology at the Roswell Park Cancer Institute in Buffalo, New York. "Since a febrile response is highly conserved in nature (even so-called cold blooded animals move to warmer places when they become ill) it would seem important that we immunologists devote more attention to this interesting response."

Scientists found that the generation and differentiation of a particular kind of lymphocyte, known as a "CD8+ cytotoxic T-cell" (capable of destroying virus-infected cells and tumor cells) is enhanced by mild fever-range hyperthermia. Specifically, their research suggests that elevated body temperature changes the T-cells' membranes which may help mediate the effects of micro-environmental temperature on cell function. To test this, researchers injected two groups of mice with an antigen, and examined the activation of T-cells following the interaction with antigen presenting cells. Body temperature in half of the mice was raised by 2 degrees centigrade, while the other half maintained a normal core body temperature. In the warmed mice, results showed a greater number of the type of CD8 T-cells capable of destroying infected cells.

"Having a fever might be uncomfortable," said John Wherry, Ph.D., Deputy Editor of the Journal of Leukocyte Biology, "but this research report and several others are showing that having a fever is part of an effective immune response. We had previously thought that the microbes that infect us simply can't replicate as well when we have fevers, but this new work also suggests that the immune system might be temporarily enhanced functionally when our temperatures rise with fever. Although very high body temperatures are dangerous and should be controlled, this study shows that we may need to reconsider how and when we treat most mild fevers."

Details: Thomas A. Mace, Lingwen Zhong, Casey Kilpatrick, Evan Zynda, Chen-Ting Lee, Maegan Capitano, Hans Minderman, and Elizabeth A. Repasky. Differentiation of CD8+ T cells into effector cells is enhanced by physiological range hyperthermia. J. Leukoc Biol November 2011 90:951-962; doi:10.1189/jlb.0511229 ; <http://www.jleukbio.org/content/90/5/951.abstract>

<http://news.discovery.com/human/human-blood-rice-dracula-111031.html>

Blood From a Stone? No. Blood From Rice? Sure

Researchers say they have found a way to produce and harvest large quantities of a blood protein from grains of rice.

Dracula may have a square meal at last. Researchers in China believe they have found a way to produce and harvest large quantities of human serum albumin (HSA) - a blood protein that is widely used in drug and vaccine production - from ordinary grains of rice. "It looks like an interesting technological step forward," Dr. Richard J. Benjamin, chief medical officer for the American National Red Cross, told FoxNews.com. "It could potentially produce large quantities in a reasonable time."

According to the study, Yang He and his colleagues discovered a way to produce the protein in rice seeds and were able to purify the HSA from it, obtaining about 2.75 grams of HSA per kilogram of rice. The protein was tested on rats and they found that the rice-produced HSA was chemically equivalent to the blood-derived version. "The disadvantage of what we currently use is that it is a blood product, which means it could transmit infection," Benjamin noted.

HSA is used in hospitals for resuscitation, when patients need fluids, when they have lost blood, or for burn victims. According to the authors of the study, the findings suggest that the transgenic rice seeds may be a cost-effective source for HSA and might help satisfy an increasing worldwide demand for the protein.

Dr. Benjamin disagrees that there is a high demand for this particular protein. "If it were to come to the market it in the USA, I just don't know that there is a screaming demand for an unmet need for HSA." He does emphasize, however, the need and demand for any and all blood donations. "Right now, all blood donations are needed desperately," said Benjamin. Though the tests on the rice are complete, this method of extracting HSA from rice has to be approved by a lengthy FDA process before it hits any market.

<http://nyti.ms/tXBmr3>

Concerns Are Raised About Genetically Engineered Mosquitoes ***These mosquitoes are genetically engineered to kill - their own children.***

By ANDREW POLLACK

Researchers on Sunday reported initial signs of success from the first release into the environment of mosquitoes engineered to pass a lethal gene to their offspring, killing them before they reach adulthood.

The results, and other work elsewhere, could herald an age in which genetically modified insects will be used to help control agricultural pests and insect-borne diseases like dengue fever and malaria.

But the research is arousing concern about possible unintended effects on public health and the environment, because once genetically modified insects are released, they cannot be recalled.

Authorities in the Florida Keys, which in 2009 experienced its first cases of dengue fever in decades, hope to conduct an open-air test of the modified mosquitoes as early as December, pending approval from the Agriculture Department.



Oxitec injected DNA into mosquito eggs to modify the species. Derric Nimmo/Oxitec

"It's a more ecologically friendly way to control mosquitoes than spraying insecticides," said Coleen Fitzsimmons, a spokeswoman for the Florida Keys Mosquito Control District.

The Agriculture Department, meanwhile, is looking at using genetic engineering to help control farm pests like the Mediterranean fruit fly, or medfly, and the cotton-munching pink bollworm, according to an environmental impact statement it published in 2008. Millions of genetically engineered bollworms have been released over cotton fields in Yuma County, Ariz.

Yet even supporters of the research worry it could provoke a public reaction similar to the one that has limited the acceptance of genetically modified crops. In particular, critics say that Oxitec, the British biotechnology company that developed the dengue-fighting mosquito, has rushed into field testing without sufficient review and public consultation, sometimes in countries with weak regulations.

"Even if the harms don't materialize, this will undermine the credibility and legitimacy of the research enterprise," said Lawrence O. Gostin, professor of international health law at Georgetown University.

The first release, which was discussed in a scientific paper published online on Sunday by the journal Nature Biotechnology, took place in the Cayman Islands in the Caribbean in 2009 and caught the international scientific community by surprise. Oxitec has subsequently released the modified mosquitoes in Malaysia and Brazil.

Luke Alphey, the chief scientist at Oxitec, said the company had left the review and community outreach to authorities in the host countries. "They know much better how to communicate with people in those communities than we do coming in from the U.K." he said.

Dr. Alphey was a zoology researcher at Oxford before co-founding Oxitec in 2002. The company has raised about \$24 million from investors, including Oxford, he said. A major backer is East Hill Advisors, which is run by the New England businessman Landon T. Clay, former chief executive of Eaton Vance, an investment management firm.

Oxitec says its approach is an extension of a technique used successfully for decades to suppress or even eradicate pests, which involves the release of millions of sterile insects that mate with wild ones, producing no offspring. But the technique has not been successfully used for mosquitoes, in part because the radiation usually used to sterilize the insects also injures them, making it difficult for them to compete for mates against wild counterparts.

Oxitec has created *Aedes aegypti* mosquitoes, the species that is the main transmitter of the dengue and yellow fever viruses, containing a gene that will kill them unless they are given tetracycline, a common antibiotic.

In the lab, with tetracycline provided, the mosquitoes can be bred for generations and multiplied. Males are then released into the wild, where tetracycline is not available. They live long enough to mate but their progeny will die before adulthood.

The study published on Sunday looked at how successfully the lab-reared, genetically modified insects could mate. About 19,000 engineered mosquitoes were released over four weeks in 2009 in a 25-acre area on Grand Cayman island.

Based on data from traps, the genetically engineered males accounted for 16 percent of the overall male population in the test zone, and the lethal gene was found in almost 10 percent of larvae. Those figures suggest the genetically engineered males were about half as successful in mating as wild ones, a rate sufficient to suppress the population. Oxitec has already said a larger trial on Grand Cayman island in 2010 reduced the population of the targeted mosquito by 80 percent for three months. That work has not yet been published.

Dr. Alphey said the technique was safe because only males were released, while only females bite people and spread the disease, adding that it should have little environmental impact. "It's exquisitely targeted to the specific organism you are trying to take out," he said.

The company is focusing on dengue fever rather than malaria because a single mosquito species is responsible for most of its spread, while many species carry malaria. Also, unlike for malaria, there are no drugs to treat dengue, and bed nets do not help prevent the disease because the mosquito bites during the day.

There are 50 million to 100 million cases of dengue each year, with an estimated 25,000 deaths. The disease causes severe flulike symptoms and occasionally, hemorrhagic fever.

The Oxitec technique, however, is not foolproof.

Alfred M. Handler, a geneticist at the Agriculture Department in Gainesville, Fla., said the mosquitoes, while being bred for generations in the lab, can evolve resistance to the lethal gene and might then be released inadvertently.

Todd Shelly, an entomologist for the Agriculture Department in Hawaii, said in a commentary published on Sunday by Nature Biotechnology that 3.5 percent of the insects in a lab test survived to adulthood despite presumably carrying the lethal gene.

Also, the sorting of male and female mosquitoes, which is done by hand, can result in up to 0.5 percent of the released insects being female, the commentary said. If millions of mosquitoes were released, even that small percentage of females could lead to a temporary increase in disease spread.

Oxitec and a molecular biologist, Anthony A. James of the University of California, Irvine, say they have developed a solution - a genetic modification that makes female mosquitoes, but not males, unable to fly. The grounded females cannot mate or bite people, and separating males from females before release would be easier.

In a test in large cages in Mexico, however, male mosquitoes carrying this gene did not mate very successfully, said Stephanie James, director of science at the Foundation for the National Institutes of Health, which oversaw the project.

In Arizona, pink bollworms sterilized by radiation have already helped suppress the population of that pest. To monitor how well the program is working, the sterile bugs are fed a red dye. That way, researchers can tell if a trapped insect is sterile or wild.

But the dye does not always show up, leading to false alarms that wild bollworms are on the loose. Giving the sterilized bugs a coral gene that makes them glow with red fluorescence is a better way to identify them, said Bruce Tabashnik, an entomologist at the University of Arizona. He is an author of a report on the field trial published in the journal PLoS One in September.

Experts assembled by the World Health Organization are preparing guidelines on how field tests of genetically modified insects should be conducted. Proponents hope the field will not face the same opposition as biotechnology crops. "You don't eat insects," said Dr. James of the Foundation for the National Institutes of Health. "This is being done for a good cause."

This article has been revised to reflect the following correction:

Correction: November 2, 2011

*A picture on Monday with an article about genetically engineered mosquitoes, using information from Oxitec, the company doing the research, misidentified the species of mosquito shown. It is a female *Aedes albopictus*, not an *Aedes aegypti*.*

More radionuclide therapy is better for prostate cancer patients

For prostate cancer patients with bone metastases, repeated administrations of radionuclide therapy with 188Re-HEDP are shown to improve overall survival rates and reduce pain, according to new research published in the November issue of The Journal of Nuclear Medicine.

Reston, Va. - Approximately 50 percent of prostate cancer patients develop bone metastases that are predominately osteoblastic, that is, have the tendency to fracture resulting in serious morbidity. This type of bone metastasis often leads to chronic pain syndrome in prostate cancer patients; as many as 50 percent of prostate cancer patients with chronic pain syndrome are reported to receive inadequate pain treatment, which makes them candidates for radionuclide therapy.

The retrospective study, "Palliation and Survival After Repeated 188Re-HEDP Therapy of Hormone-Refractory Bone Metastases of Prostate Cancer: A Retrospective Analysis," reviewed cases of 60 patients with hormone-refractory prostate cancer. The patients, all of whom had more than five lesions documented by a bone scan, were divided into three groups - those who received one therapy, two therapies or three or more therapies.

"Radionuclide therapy of bone metastases has been used for several decades for those with prostate cancer," noted lead author of the study Hans-Juergen Biersack, MD. "For this study, we developed 188Re-HEDP as a novel radiopharmaceutical which - due to its short half life of 19 hours - makes sequential therapy possible."

The researchers found that post-treatment survival increased with the number of radionuclide therapies administered. Patients with progressive hormone-refractory prostate cancer receiving one therapy added 4.5 months, those receiving two therapies added 10 months, and those receiving three or more therapies improved their survival by 15.7 months. In addition, while the Gleason scores - a grading system used to evaluate the prognosis of men with prostate cancer - for each group were similar, the number of life-lost years for patients receiving three or more therapies was significantly lower.

In regards to pain reduction, no significant difference was found among those receiving 188Re-HEDP therapies. Pain reduction was achieved in 89.5 percent of those receiving one therapy, in 94.7 percent of those receiving two therapies and in 90.9 percent of those receiving three or more therapies.

"For patients failing chemotherapy or hormone treatments, 188Re-HEDP is a promising therapy that can both extend the number of survival years and help relieve pain from bone metastases," noted Biersack. "The findings support and expand the role of molecular therapy with radioisotopes in oncology."

188Re-HEDP is not commercially available and in-house production is required. 188Re-HEDP treatments for this study were developed at Oak Ridge National Laboratory in Oak Ridge, Tenn.

Authors of the article "Palliation and Survival After Repeated 188Re-HEDP Therapy of Hormone-Refractory Bone Metastases of Prostate Cancer: A Retrospective Analysis" include: Hans-Juergen Biersack, Holger Palmedo, Andrej Andris, Stefan Guhlke, Samer Ezziddin, Jan Bucerius and Dirk von Mallek, Department of Nuclear Medicine, University of Bonn, Bonn, Germany; Stefan Rogenhofer, Department of Urology, University Hospital Bonn, Bonn, Germany; and Furn F. Knapp, Nuclear Medicine Program, Oak Ridge National Laboratory, Oak Ridge, Tennessee.

<http://nyti.ms/rP0pJJ>

Turkey: Sandblasting Jeans for 'Distressed' Look Proved Harmful for Textile Workers

Sandblasting new blue jeans to make them look "distressed" killed a number of young Turkish textile workers before the practice was outlawed, a new study has found.

By DONALD G. McNEIL Jr.

The study, published in *Chest*, a medical journal for lung specialists, was done by doctors at a hospital for thoracic diseases in Istanbul. They followed 32 male textile workers who came to their hospital with breathing problems between 2001 and 2009. That year, after news reports of a "silicosis epidemic," Turkish health authorities banned sandblasting denim.

The men were young, with a mean age of 31. Most were previously healthy; they were screened to rule out damage from tuberculosis or smoking. They had worked a mean of 66 hours a week for a little over two years each, mostly at small sandblasting shops with fewer than 10 workers.

Six of the workers died, and 16 others had disabling lung damage from breathing the fine sand. The researchers calculated that a typical worker with silicosis had only a 69 percent chance of surviving five years.

Although more former sandblasters will suffer lung deterioration, the new ban increased awareness and "may prevent new silicosis cases in Turkey," the authors wrote.

Since the blasting serves no purpose other than to satisfy fashion whims, the scientists called for a global campaign against it.

No Higher Risk of Breast Cancer for Women Who Don't Have BRCA Mutation but Have Relatives Who Do

Women related to patients with breast cancer caused by a hereditary mutation - but don't have the mutation themselves - have no higher cancer risk than relatives of patients with other types of breast cancer

ScienceDaily - In the largest study of its kind to date, Stanford University School of Medicine researchers have shown that women related to a patient with a breast cancer caused by a hereditary mutation - but who don't have the mutation themselves - have no higher risk of getting cancer than relatives of patients with other types of breast cancer. The multinational, population-based study involving more than 3,000 families settles a controversy that arose four years ago when a paper hinted that a familial BRCA mutation in and of itself was a risk factor.

"The results are encouraging and reassuring," said Allison Kurian, MD, assistant professor of oncology and of health research and policy and first author of a paper that appears online Oct. 31 in the *Journal of Clinical Oncology*. She and her colleagues - including senior author Alice Whittemore, PhD, professor of health research and policy - said their findings support the current practice of advising so-called non-carriers that there is no increase in risk attributable to their family-specific BRCA1 or BRCA2 mutation.

The study doesn't dispute that women who have relatives with any type of breast cancer have a greater risk of contracting the disease compared to those with no cancer-stricken relatives.

Mutations in the BRCA1 and BRCA2 genes are strongly associated with the development of breast or ovarian cancer: Carriers face a five- to 20-fold increased risk of developing these cancers and are usually subject to intensive screening and risk-reduction strategies. Female relatives who are tested and found not to carry the family-specific mutation have historically been advised that their cancer risks are the same as those of other relatives of breast cancer patients (that is, slightly higher than women in the general population).

The field was shaken up when a 2007 *Journal of Medical Genetics* paper showed that women who tested negative for a familial BRCA mutation had a two- to five-fold increased risk of developing breast cancer. Several other studies found a two-fold risk for non-carriers who had a relative with the mutation, prompting some to wonder whether ongoing breast cancer surveillance should be recommended for these relatives.

"Our clinic received many calls about it - it was widely read by people in the field and by patients," said Kurian, a practicing oncologist whose research focuses on breast cancer risks across populations. The study, and the notion that additional screening for non-carriers might be warranted, caused both concern and skepticism among cancer geneticists. "It went against what was being done."

The 2007 study had compared relatives of BRCA carriers with women in the general population, and Kurian and her colleagues thought this might have created high estimates of the non-carriers' risk. For one reason: Women in a family with a known BRCA mutation are more likely to receive more intensive screening, and thus be more likely to be diagnosed with breast cancer than women in the general population.

And also, said Whittemore, "First-degree relatives of breast cancer patients are themselves at higher risk than women in the general population. So some reports of higher risk among non-carriers, as compared to risk in the general population, may have been an inappropriate comparison of apples and oranges."

The researchers sought, then, to compare cancer risk in non-carriers with a control group of relatives of cancer patients without the mutations. For the study they used data from population-based cancer registries provided by co-investigators from the Cancer Prevention Institute of California, the University of Melbourne in Australia and the University of Toronto in Canada to look at 3,047 families. Of the total, 160 families had BRCA1 and 132 had BRCA2 mutations.

When comparing the groups of relatives, they found no evidence of an increased breast cancer risk for non-carriers compared with the control group. The authors note that this finding supports "evidence-based practice guidelines [that] currently recommend that non-carriers be screened according to standard protocols for their age and other risk factors."

The findings should put to rest questions about risk based on a familial BRCA mutation. But Kurian added, "It's important for patients and clinicians to remember this doesn't rule out other risk factors, which might increase a non-carrier's probability of getting breast cancer."

Other co-authors include Gail Gong, PhD, senior research scientist; Esther John, PhD, senior research scientist at the Cancer Prevention Institute of California and consulting professor of health research and policy at Stanford; programmers David Johnston and Anna Felberg; and Dee West, PhD, emeritus professor of health research and policy at Stanford and senior advisor at the CPIC.

Funding came from the National Cancer Institute, National Institutes of Health, Cancer Care Ontario, CPIC and the University of Melbourne, and through cooperative agreements with members of the Breast Cancer Family Registry and principal investigators.

http://www.eurekalert.org/pub_releases/2011-11/plos-awu103111.php

A widely used bee antibiotic may harm rather than help

Honey bee populations have been mysteriously falling for at least five years in the United States, but the cause of so-called colony collapse disorder (CCD) is still largely unknown.

In a report published Nov. 2 in the online journal PLoS ONE, researchers report that a widely used in-hive medication may make bees more susceptible to toxicity of commonly used pesticides, and that this interaction may be at least partially responsible for the continuing honey bee population loss.

The researchers, led by David Hawthorne of University of Maryland, pre-treated healthy honey bees with the antibiotic oxytetracycline, and then exposed the bees to two pesticides that are commonly used in bee hives to control parasitic varroa mites. In both cases, the pre-treated bees were much more sensitive to pesticide exposure than were bees that had not been treated.

The team suspected that oxytetracycline may interact with specific bee proteins called multiple drug resistance (MDR) transporters, making them less effective and therefore rendering the bee more at risk to the pesticides. To test this hypothesis, they pre-treated the bees with another drug, verapamil, which is known to inhibit a particular MDR transporter. These insects showed increased sensitivity to five different pesticides, supporting the group's theory that MDR transporters, and specific combinations of independently safe chemicals, may play an important role in CCD.

Citation: Hawthorne DJ, Dively GP (2011) 'Killing Them with Kindness? In-Hive Medications May Inhibit Xenobiotic Efflux Transporters and Endanger Honey Bees'. PLoS ONE 6(11): e26796. doi:10.1371/journal.pone.0026796

Financial Disclosure: This work was supported by the United States Department of Agriculture. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

http://www.eurekalert.org/pub_releases/2011-11/sumc-cu110111.php

Continuous use of nitroglycerin increases severity of heart attacks, Stanford study shows

When given for hours as a continuous dose, the heart medication nitroglycerin backfires - increasing the severity of subsequent heart attacks, according to a study of the compound in rats by researchers at the Stanford University School of Medicine.

STANFORD, Calif. - "Basically it's a cautionary tale," said professor of chemical and systems biology Daria Mochly-Rosen, PhD, senior author of the study that will be published Nov. 2 in Science Translational Medicine. "Here is a practice in medicine used for over 100 years. Nitroglycerin is so old that a proper clinical trial has never been formally done. Our study says it's time for cardiologists to examine the value of nitroglycerin treatment that extends for hours at a time."

The study also showed that the damage can be reduced by simultaneous treatment with an enzyme activator known as Alda-1, discovered by Mochly-Rosen and collaborators and reported in Science in 2008.

Nitroglycerin is a mainstay of care for heart disease. It's the go-to medicine for those suffering from bouts of chest pain, known as angina pectoris, who take it as a sublingual tablet or oral spray. And it's a standard treatment for heart attack patients, who get it also through an I.V. drip or patch in the emergency room.

It works like a charm, at least at first, opening vessels so blood can flow to the heart more easily. But sustained use leads to desensitization, a pitfall noticed shortly after the explosive chemical was first used as a drug, in 1867 - the same year Alfred Nobel obtained his patents for dynamite, which had nitroglycerin as its main ingredient. To reduce desensitization to nitroglycerin, modern physicians cycle patients on and off the drug: A typical regimen for hospitalized heart attack patients is 16 hours on, eight hours off. An occasional tablet or spritz is not known to lead to this dampened response.

What wasn't suspected until the last decade was that prolonged use of nitroglycerin could actually harm heart tissue if a heart attack occurs. Among the evidence are observations that nitroglycerin damages cells in the heart by wrecking an important enzyme, ALDH2, which not only mops up toxic products of free radicals, but is the key to nitroglycerin's ability to stave off chest pain. ALDH2 catalyzes the conversion of nitroglycerin to nitric oxide, which reduces chest pain by opening the blood vessels. So by damaging ALDH2, nitroglycerin shoots itself in the foot as a heart disease treatment.

In 2008, Mochly-Rosen and colleagues identified another function of ALDH2: It's a critical enzyme for protecting the heart from damage caused by ischemia, or decreased blood flow - not just for people being treated with nitroglycerin, but for everyone. So the researchers too became concerned about the safety of sustained nitroglycerin use.

"We knew that nitroglycerin was an important treatment for heart attack symptoms," said Mochly-Rosen, who is also the George D. Smith Professor in Translational Medicine. "And we thought, 'Wait, everyone gets nitroglycerin when they come to the emergency room with chest pains, sometimes in a drip or as a patch. What if they get a heart attack during this period? It could be more severe than if they had not been treated.'"

That led to their current study. Using a rat model, they tested the effect of sustained nitroglycerin treatment on the severity of heart attacks. They found that nitroglycerin increased heart attack severity in rats. After 16 hours of nitroglycerin treatment, the heart damage was twice as large as in untreated control animals. Five to eight animals made up each group.

Cardiac function was also significantly diminished in relation to the control animals, as determined by echocardiograms immediately after the heart attack and again two weeks later. And when the rats were given the enzyme activator Alda-1 along with nitroglycerin, the detrimental effects of prolonged nitroglycerin treatment were nearly erased. "We showed unequivocally that the rats were worse off after nitroglycerin treatment, and if we had Alda-1 on board, we protected them," said Mochly-Rosen.

"Nitroglycerin improves blood flow when the vessels are constricting. But what we found is that if you use it for too long, the enzyme that helps protect against tissue damage - ALDH2 - dies. With our animal model, we demonstrated that the loss of this enzyme makes the outcome from the heart attack worse. Nitroglycerin is not benign."

Given the importance of ALDH2 in protecting different tissues, including the heart, nitroglycerin tolerance should not be considered as a simple loss of drug efficacy, said co-author Julio Cesar Batista Ferreira, PhD, a postdoctoral scholar. "Our study was the first to show the nitroglycerin tolerance is associated with increased cardiac vulnerability. Further studies to identify the molecular mechanisms of nitroglycerin tolerance and its side effects are needed."

Alternative treatments to improve blood flow in cardiac patients exist, said cardiologist John Cooke, MD, PhD, a Stanford professor of cardiovascular medicine who was not involved in the study but has discussed it with the researchers. "Continuous administration of nitroglycerin by patch or by intravenous infusion, as in the coronary care unit, is initially useful in relieving pain and also favorably influences hemodynamics - reduces blood pressure, improves coronary blood flow. However, extended use of this form of nitroglycerin is known to induce tolerance to its own beneficial actions within 12 to 24 hours," said Cooke, adding that researchers don't yet know the full effects of using the drug for more than 24 hours.

"Professor Mochly-Rosen's work raises additional concern about the extended use of long-acting or continuous administration of nitroglycerin in the coronary care unit," he added. "It is probably best to use nitroglycerin continuously for only short periods of time, and replace the continuous infusion or patch with other medications to reduce symptoms and favorably influence hemodynamics."

In the future, said Mochly-Rosen, nitroglycerin could be made safe by pairing it with Alda-1, if it is proven safe in humans, or another drug with a similar enzyme-activating function.

Mochly-Rosen's collaborators were Ferreira and first author Lihan Sun, PhD, a former graduate student.

The research was supported by the National Institute on Alcohol Abuse and Alcoholism and the São Paulo Research Foundation. A patent has been filed by Stanford University for the therapeutic use of Alda-1 to target ALDH2 and treat myocardial ischemia. Mochly-Rosen is the founder of ALDEA Pharmaceuticals Inc. and KAI Pharmaceuticals Inc., which she reports have no current plans to develop products in connection with this research.

Information about Stanford's Department of Chemical and Systems Biology, which also supported the work, is available at <http://casb.stanford.edu/>.

<http://www.physorg.com/news/2011-11-queen-english.html>

'Queen's English' not the best

Native English speakers should give up their claim to be the guardians of the purest form of the language and accept that the ways it is used and changed by millions around the world are equally valid.

A linguist at the University of Portsmouth, Dr. Mario Saraceni, has published an article in the latest issue of the journal *Changing English* which suggests the way English is taught to non-native speakers and the attitudes of those for whom it is their mother tongue need a dramatic change. He said: "It's important the psychological umbilical cord linking English to its arbitrary centre in England is cut. The English are not the only legitimate owners of the language. "English is the most dominant language on the planet and though it is spoken widely in the western world, westerners are in the minority of English language speakers.

"For many around the world, the ability to speak English has become as important as knowing how to use a computer. But the myth of the idealized native speaker needs to be abandoned. How it is spoken by others should not be seen as second best."

Dr. Saraceni, of the School of Languages and Area Studies, said it was time English language teachers abroad took down posters of double-decker buses and Parliament Square from their classrooms and taught English in a purely local context. He said: "Critics might feel uncomfortable with what they see as a laissez-faire attitude but language use is not about getting closer to the 'home' of English, and it is not about bowing deferentially and self-consciously to the so-called superiority of the inner circle of the UK, US, Australia and New Zealand. "Language use is fundamentally about mutual understanding."

According to Dr Saraceni, the widely held view that English has spread around the world from its original birthplace in England can be challenged. "The idea seems natural and unquestionable, but if you examine it closer it is patently untrue. It is impossible to identify any point in history or geography where the English language started - one can talk only of phases of development. The origins of English are not to be found in the idea of it spreading from the centre to the periphery, but in multiple, simultaneous origins. The concept of a single version of any language is always questionable."

English has been "reincarnated" throughout the world, including in Malaysia, India, China and Nigeria but England should not be seen as the linguistic "garden of Eden" where the language was pure and perfect, he said, though this notion has "not yet been accepted by linguistic vigilantes or the power elite" despite being favoured by many linguists globally. The de-Anglicisation of English needs to take place primarily in classrooms and the "whole mystique of the native speaker and mother tongue should be quietly dropped from the linguist's set of myths about the language".

Dr. Saraceni said: "Fundamentally, we need to re-think the whole concept of languages in connection to nations and we need to begin to accept that people use the linguistic repertoires that suit them the most. The notion of separate of language 'A', language 'B', etc. needs to be reconsidered in favor of a more flexible approach." Dr. Saraceni's thought piece is published in the latest issue of Changing English.

Provided by University of Portsmouth

http://www.eurekalert.org/pub_releases/2011-11/ps-hac102811.php

Humans and climate contributed to extinctions of large ice-age mammals, new study finds

Both climate change and humans were responsible for the extinction of some cold-adapted animals and the near extinction of others

The history of six large herbivores - the woolly rhinoceros, woolly mammoth, wild horse, reindeer, bison, and musk ox - is the subject of a study by an international group of scientists investigating how climate fluctuations and human activity affected mammal populations at the end of the last ice age. According to Beth Shapiro, the Shaffer Associate Professor of Biology at Penn State University and a member of the research team, both climate change and humans were responsible for the extinction of some cold-adapted animals and the near extinction of others. The results of the study, which is the first to use genetic, archeological, and climatic data together to infer the population history of large-bodied Ice-Age mammals, will be published in the journal Nature. The study's findings are expected to shed light on the possible fates of living species of mammals as our planet continues its current warming cycle.

Shapiro explained that all six of the species her team studied flourished during the Pleistocene Epoch - the period of geological time that lasted from about 2 million to 12,000 years ago. "During this time, there were lots of climatic ups and downs - oscillations between long, warm intervals called interglacial periods, during which the climate was similar to what we have today, followed by long, cold intervals called glacial periods, or ice ages," Shapiro said. "Although these cold-adapted animals certainly fared better during the colder, glacial periods, they still managed to find places where the climate was just right - refugia - so that they could survive during the warmer, interglacial periods. Then, after the peak of the last ice age around 20,000 years ago, their luck started to run out. The question is, what changed? Why were these mammals no longer able to find safe refugia where they could survive in a warm climate?"

To answer these questions, Shapiro and her team collected many different types of data to test hypotheses about how, when, and why the woolly rhinoceros, woolly mammoth, and wild horse all went extinct after the last ice age, and why the reindeer, bison, and musk ox were able to survive - albeit in much more restricted ranges than they could inhabit during the ice ages. "One source of information we used was DNA from the animals themselves," Shapiro explained. "With genetic data, it's possible to estimate when and how much populations were able to grow and shrink as the climate changed and their habitat started to disappear." The team also collected climatic data - temperature and precipitation patterns - from both glacial and interglacial periods, as well as archeological data, which they used to study the extent to which early humans may have

influenced the survival of these six mammal species. "For example, in locations where animal bones had been cooked or converted into spears, we know that humans lived there and were using them as a resource," Shapiro said. "Even where we don't find evidence that humans were using the animals, if humans and the animals lived in the same place and at the same time, humans could have had some influence on whether the animals survived or not."

In the case of the now-extinct woolly rhinoceros, the scientists found that, in Europe, the ranges of humans and woolly rhinoceros never overlapped. "These data suggest that climate change, and not humans, was the main reason why this particular species went extinct in present-day Europe," Shapiro said. "Still, we expect humans might have played a role in other regions of the world where they did overlap with woolly rhinos, and so further studies will be necessary to test this hypothesis." Much clearer was the evidence that humans did influence, and not always negatively, the population sizes of the five other species - the woolly mammoth, wild horse, reindeer, bison, and musk ox.

Shapiro explained that population fluctuations for all six species continued until the end of the last ice age - around 14,000 years ago - when many of the species simply disappeared. "The take-home message is that during the most recent warming event, when the last ice age faded into the warm interval we have today, something kept these animals from doing what they had always done, from finding alternative refugia - less-than-ideal, but good-enough chunks of land on which to keep their populations at a critical mass," Shapiro said. "That 'something' was probably us - humans." During the period when these animals were declining, the human population was beginning its boom, and was spreading out across not only the large-bodied mammals' cold-climate habitats, but also across their warm-climate refuges, changing the landscape with agriculture and other activities. Many large-bodied, cold-adapted mammals, including the horse - which is considered extinct in the wild and now survives only as a domesticated animal - suddenly had no alternative living spaces, and, as such, no means to maintain their populations.

"The results of our study suggest that although past warm periods caused these animal species to go through periodic bottlenecks - evolutionary events during which the size of a population diminishes substantially and stays small for a long time - they always seemed to bounce back, and to return to their previous habitats as soon as the Earth became cooler again. Then, during the most-recent warming cycle, that trend changed," Shapiro said.

As the climate became warmer after the last ice age, the woolly rhinoceros, woolly mammoth, and wild horse became extinct, and the reindeer, bison, and musk ox may have just been fortunate in avoiding extinction, according to Shapiro. Reindeer managed to find safe habitat in high arctic regions and, today, have few predators or competitors for limited resources. Bison are extinct in Asia, where their populations were extensive during the ice ages, and today they are found only in North America, although a related species survives in small numbers in Europe. Cold-adapted muskoxen now live only in the arctic regions of North America and Greenland, with small introduced populations in Norway, Siberia, and Sweden. Interestingly, if humans had any impact on musk-ox populations, it may have been to help sustain them. Musk-ox populations first became established in Greenland around 5,000 years ago, after which they expanded rapidly, despite having been a major resource for the Paleo-Eskimo population. Today, the animal species survives in large numbers.

Shapiro also said that her team's findings could help to predict the fate of populations threatened by the climate change and habitat alteration that is happening today. "Our results provide direct evidence that something changed between the most-recent glacial cycle, when many of these species went extinct, and previous glacial cycles, through which they all managed to survive. Although it is clear that climate change drives the dynamics of these species, we, as humans, have to take some of the blame for what happened during this most-recent cycle. It seems that our ancestors were able to change the landscape so dramatically that these animals were effectively cut off from what they needed to survive, even when the human population was small," Shapiro said. "There are many more humans today, and we have changed and are continuing to change the planet in even more important ways."

In addition to Shapiro, many other scientists contributed to this study. In the United States, contributing authors are from institutions in Utah, California, Texas, Missouri, Maryland, Colorado, Massachusetts, Oregon, and Kansas. The study's international contributors are from institutions in Denmark, Australia, Sweden, Spain, the United Kingdom, the Netherlands, Germany, Norway, Russia, China, and Canada.

The research was funded, in part, by the Leverhulme Trust, the Awards Fund, the Danish National Research Foundation, the Lundbeck Foundation, the Danish Council for Independent Research, and the U.S. National Science Foundation.

In Some Cases, Even Bad Bacteria May Be Good
***THE HYPOTHESIS* Overuse of antibiotics increases the risk of obesity.**
***THE INVESTIGATOR* Dr. Martin Blaser, New York University Langone Medical Center.**
By KATE MURPHY

Overuse of antibiotics has led to the creation of drug-resistant bacteria - so-called superbugs, like methicillin-resistant staphylococcus aureus. But now some researchers are exploring an equally unsettling possibility: Antibiotic abuse may also be contributing to the increasing incidence of obesity, as well as allergies, inflammatory bowel disease, asthma and gastroesophageal reflux.

Among those sounding the alarm is Dr. Martin Blaser, a professor of microbiology at New York University Langone Medical Center. In a commentary published in August in the journal *Nature*, he asserted that antibiotics are permanently altering microbial flora of the human body, also known as the microbiome or microbiota, with serious health consequences.

The human gut in particular is home to billions of bacteria, but little is known about this hidden ecosystem. Take *Helicobacter pylori*, a bacterium associated with an increased risk of ulcers and gastric cancer. Many doctors are quick to prescribe antibiotics to kill it even when the patient has no symptoms.

But in 1998, in a paper published in the *British Medical Journal*, Dr. Blaser was more circumspect, arguing that *H. pylori* might not be such a bad actor after all. "We're talking about a bug that's been in the human gut for at least 58,000 years," Dr. Blaser said in an interview. "There's probably a reason for that."

His lab has since produced a stream of findings supporting his suspicion. Dr. Blaser and his colleagues discovered, for instance, that the stomach behaves differently after a course of antibiotics eradicates resident *H. pylori*. After a meal, levels of ghrelin, a hunger hormone secreted in the stomach, are supposed to fall. But in subjects without *H. pylori*, the amount of ghrelin in the bloodstream held steady, in essence telling the brain to keep eating. Moreover, mice in Dr. Blaser's lab fed antibiotics in dosages similar to those given to children to treat ear and throat infections - which is enough to kill *H. pylori* in many patients - had marked increases in body fat even though their diets remained the same. (Indeed, farmers have long given antibiotics to livestock to promote weight gain without increasing caloric intake.)

These results dovetail with research by Peter Turnbaugh, a Harvard University geneticist, in collaboration with Dr. Jeffrey Gordon, a gastroenterologist at Washington University in St. Louis. They have found that the ratios of various bacteria in the guts of obese mice and obese humans were significantly different from those of lean controls, suggesting that altering the stomach's microbial balance with antibiotics might put patients at risk for gaining weight.

Antibiotic overuse may be the root of other health problems, too. An epidemiologist at New York University, Yu Chen, has found an inverse correlation between *H. pylori* infection and childhood-onset asthma, hay fever and skin allergies in 7,600 participants in the National Health and Nutrition Survey.

Observation research has shown that the elimination of *H. pylori* actually increases the risk of gastric reflux, which is itself associated with asthma as well as esophageal diseases. Researchers in Switzerland and Germany have reported that mice given *H. pylori* actually are protected against asthma.

Dr. Barry Marshall, the professor of clinical biology at the University of Western Australia in Perth who was awarded the Nobel Prize in Medicine in 2005 for his part in the discovery of *H. pylori* and its role in gastritis and peptic ulcer disease, had a more measured reaction. "I've never killed anyone giving them antibiotics for *H. pylori*, but people have been killed who didn't get antibiotics to get rid of it," he said.

Patients whose internal flora are disrupted by antibiotics tend to reacquire the bugs over time, particularly if the person lives with others, Dr. Marshall said. Nevertheless, he agreed with Dr. Blaser that antibiotics are overused and even said he foresaw a day when a detoxified strain of *H. pylori* might be administered as a treatment for conditions like obesity and asthma.

But wider use of antibiotics may be wreaking havoc far beyond that resulting from the loss of *H. pylori*. "We have so far focused on *H. pylori* because we have the diagnostic tests to detect it, but you could say *H. pylori* is an indicator organism for what is probably a vast and disappearing microbiota and increasing disease risk," said Dr. Blaser.

The National Institutes of Health shares his concern, not only awarding him a \$6.5 million grant last year to investigate the role of the disappearing microbiota in the current obesity epidemic but also allocating \$115 million in 2008 to fund the Human Microbiome Project, which proposes to identify microbes that reside on and within a healthy human being. "You can think of it as the second human genome project, where we will sequence the genes of the tremendous diversity of bacteria that populate our bodies," said Julie Segre, senior

investigator at the N.I.H.'s Human Genome Research Institute. "We will take samples from 200 healthy volunteers to get an idea of what is a normal, healthy microbiota."

It's an ambitious project, given that bodily bacteria outnumber human cells 10 to one. But researchers involved in the effort said advances in DNA sequencing technology make it an achievable goal. The effort is so far focusing only on microbes on the skin and in the nose, mouth, gut and genital area.

Dr. David Relman, professor of microbiology and immunology at Stanford University, said the Human Microbiome Project is important because it's not just antibiotics that are changing the human microbiota: "Many aspects of modern life, including diet, smaller families, more hygienic practices and improved public sanitation, are affecting our bacterial communities."

Getting a genetic snapshot of bacteria populating humans today would provide a benchmark for tracking further degradation and resulting disorders. "We need to get an understanding of how our microbial communities operate and what to feed them so they will bloom again," said Dr. Relman. "It's intriguing and entirely possible that in the future we will get a cocktail of strains and species of bacteria to repair the collateral damage that antibiotics and other practices have done to our inner ecology."

Dr. Blaser's ideas have not always been popular, but he is gratified by the gathering interest in the human microbiome and its links to health. "I know I am now doing the most important work of my career," he said.

http://www.eurekalert.org/pub_releases/2011-11/cums-npb110211.php

Nicotine primes brain for cocaine use: Molecular basis of gateway sequence of drug use

Nicotine causes specific changes in the brain that make it more vulnerable to cocaine addiction

Cigarettes and alcohol serve as gateway drugs, which people use before progressing to the use of marijuana and then to cocaine and other illicit substances; this progression is called the "gateway sequence" of drug use. An article in *Science Translational Medicine* by Amir Levine, MD, Denise Kandel, PhD; Eric Kandel, MD; and colleagues at Columbia University Medical Center provides the first molecular explanation for the gateway sequence. They show that nicotine causes specific changes in the brain that make it more vulnerable to cocaine addiction - a discovery made by using a novel mouse model.

Alternate orders of exposure to nicotine and cocaine were examined. The authors found that pretreatment with nicotine greatly alters the response to cocaine in terms of addiction-related behavior and synaptic plasticity (changes in synaptic strength) in the striatum, a brain region critical for addiction-related rewards. On a molecular level, nicotine also primes the response to cocaine by inhibiting the activity of an enzyme - histone deacetylase - in the striatum. This inhibition enhances cocaine's ability to activate a gene called FosB gene, which promotes addiction.

The relationship between nicotine and cocaine was found to be unidirectional: nicotine dramatically enhances the response to cocaine, but there is no effect of cocaine on the response to nicotine. Nicotine's ability to inhibit histone deacetylase thus provides a molecular mechanism for the gateway sequence of drug use.

Nicotine enhances the effects of cocaine only when it is administered for several days prior to cocaine treatment and is given concurrently with cocaine. These findings stimulated a new analysis of human epidemiological data, which shows that the majority of cocaine users start using cocaine only after they have begun to smoke and while they are still active smokers. People who begin using cocaine after they've started smoking have an increased risk of cocaine dependency, compared with people who use cocaine first and then take up smoking.

"These studies raise interesting questions that can now be explored further in animal models," said study author Denise Kandel, a professor of Sociomedical Sciences at the Mailman School of Public Health. "Do alcohol and marijuana - the two other gateway drugs - prime the brain by the same mechanism as nicotine? Is there a single mechanism for all gateway sequences, or does each sequence utilize a distinct mechanism?"

The results also emphasize the need for developing effective public health prevention programs encompassing all nicotine products, especially those targeted toward young people. Effective interventions not only would prevent smoking and its negative health consequences but could also decrease the risk of progression to chronic use of illicit drugs.

http://www.eurekalert.org/pub_releases/2011-11/nioa-nso110211.php

NIH scientists outline steps toward Epstein-Barr virus vaccine

Vaccine could prevent mononucleosis and cancers linked to virus

WHAT: Epstein-Barr virus (EBV) infects nine out of ten people worldwide at some point during their lifetimes.

Infections in early childhood often cause no disease symptoms, but people infected during adolescence or young adulthood may develop infectious mononucleosis, a disease characterized by swollen lymph nodes, fever

and severe fatigue. EBV also is associated with several kinds of cancer, including Hodgkin lymphoma and stomach and nasal cancers. Organ transplant recipients and people infected with HIV (who become infected with or who already are infected with EBV) also may develop EBV-associated cancers. There is no vaccine to prevent EBV infection and no way for doctors to predict whether an EBV-infected person will develop virus-associated cancer.

In a new article from the National Institutes of Health (NIH), Anthony S. Fauci, M.D., director of the National Institute of Allergy and Infectious Diseases (NIAID), and Harold Varmus, M.D., director of the National Cancer Institute (NCI), join Gary Nabel, M.D., Ph.D., director of NIAID's Vaccine Research Center, and Jeffrey Cohen, M.D., chief of NIAID's Laboratory of Infectious Diseases, in summarizing a recent meeting of experts who gathered to map directions toward an EBV vaccine. Although it may not be possible to create a vaccine that completely prevents EBV infection, the authors note, clinical observations and results from clinical trials of an experimental EBV vaccine suggest that it may be possible to create an EBV vaccine capable of preventing the diseases that sometimes follow EBV infection.

Priorities for future research include determining which immune system responses to vaccination correlate with protection from infection or disease; identifying biological markers that would enable clinicians to predict development of EBV-related cancers; and establishing collaborations among government, academic and industry scientists to further improve an experimental EBV vaccine and to spur development of second-generation EBV vaccines.

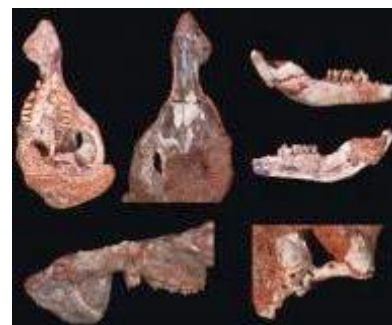
ARTICLE: *Ji Cohen et al. Epstein-Barr virus: An important vaccine target for cancer prevention. Science Translational Medicine DOI: 10.1126/scitranslmed.3002878 (2011).*

http://www.eurekalert.org/pub_releases/2011-11/uol-usd103111.php

UofL scientist discovers first known mammalian skull from Late Cretaceous in South America

Finding to be published in Nature provides important new information on evolution of mammals

LOUISVILLE, Ky. - Paleontologist Guillermo Rougier, Ph.D., professor of anatomical sciences and neurobiology at the University of Louisville, and his team have reported their discovery of two skulls from the first known mammal of the early Late Cretaceous period of South America. The fossils break a roughly 60 million-year gap in the currently known mammalian record of the continent and provide new clues on the early evolution of mammals. Details of their find will be published Nov. 3 in *Nature*. Co-authors are Sebastián Apesteguía of Argentina's Universidad Maimónides and doctoral student Leandro C. Gaetano.



Paleontologist Guillermo Rougier, Ph.D., professor of anatomical sciences and neurobiology at the University of Louisville, and his team have reported their discovery of two skulls from the first known mammal of the early Late Cretaceous period of South America. The new critter, named Cronopio dentiacutus by the paleontologists, is a dryolestoid, an extinct group distantly related to today's marsupials and placentals. Credit: University of Louisville

The new critter, named "Cronopio dentiacutus" by the paleontologists, is a dryolestoid, an extinct group distantly related to today's marsupials and placentals. "Dr. Rougier and his colleagues truly have made an outstanding discovery of the first really informative skull remains belonging to a key mammalian group," said Rich Cifelli, Ph.D., Presidential Professor of Zoology at the University of Oklahoma and a researcher who, like Rougier, has spent his career discovering and identifying mammal remains.

"The discovery of 'Cronopio' is especially notable because it provides for the first time the whole cranial morphology (form and structure) of a dryolestoid," writes Christian de Muizon, director of the Muséum National d'Histoire Naturelle in Paris in a "News and Views" article in the same issue of *Nature*.

"Cronopio" was shrew-sized, about 4-6 inches in length, and was an insectivore with a diet of the insects, grubs and other bugs of the time. It lived when giant dinosaurs roamed the earth - more than 100 million years ago - and made its home in a vegetated river plain.



Scratt

The skulls reveal that "Cronopio" had extremely long canine teeth, a narrow muzzle and a short, rounded skull. "These first fossil remains of dryolestoids ... give us a complete picture of the skull for the group," John R. Wible, Ph.D., curator of mammals at the Carnegie Museum of Natural History, said. "The new dryolestoid, 'Cronopio,' is without a doubt one of the most unusual mammals that I have seen, extinct or living, with its

elongate, compressed snout and oversized canine teeth. What it did with that unusual morphology perhaps may come to light with additional discoveries... ."

Rougier describes "Cronopio" in a manner that fans of a popular animated movie series can easily understand. "It looks somewhat like Scrat, the saber-toothed squirrel from 'Ice Age,' " he said. Cartoon references aside, Rougier, Apesteguía and Gaetano realized almost immediately the importance of the discovery when they located the fossils in 2006 because mammalian skulls are very fragile, small and rarely found.

The skulls were embedded in rock in a remote area of northern Patagonia, about 100 miles from the city of Allen in the Argentinian province of Rio Negro. Removal of the specimens from the rocks encasing them took several years of patient lab work, which eventually confirmed that the skulls were the first of their kind found.

"We knew it was important, based on the age of the rocks and because we found skulls," Rougier said. "Usually we find teeth or bone fragments of this age. Most of what we know of early mammals has been determined through teeth because enamel is the hardest substance in our bodies and survives well the passage of time; it is usually what we have left to study.

"The skull, however, provides us with features of the biology of the animal, making it possible for us to determine this is the first of its kind dating to the early Late Cretaceous period in South America," he said. "This time period in South America was somewhat of a blank slate to us. Now we have a mammal as a starting point for further study of the lineage of all mammals, humans included."

The prospects for further investigation are exciting. "In recent years it has become clear that southern continents hosted their own endemic groups of mammals during the Age of Dinosaurs. But until now, all we have had are isolated teeth and a few jaw fragments ... which don't really help much in deciphering broader relationships," Cifelli said. "For this reason, the new fossils provide a sort of Rosetta Stone for understanding the genealogy of early South American mammals, and how they fit in with those known from northern landmasses. Now the burden is on the rest of us to find similarly well preserved fossils from elsewhere, so that the broader significance of Rougier's finds can be fully placed in context."

In addition to conducting research, Rougier teaches anatomy to UofL School of Medicine students and said the discovery extends the knowledge of our lineage.

"This tells us a little more of the full history of our lineage, a very resilient lineage," he said. " 'Cronopio' lived in a completely different world than ours, dominated by dinosaurs and with a different geography; these new fossils give us information on how transient and ever-evolving our world is."

Rougier, a native Argentinian, earned his doctorate at Universidad de Buenos Aires and joined the UofL faculty in 1998 following work at the American Museum of Natural History in New York and Museo Argentino de Ciencias Naturales in Buenos Aires. Funding to support his work came from the National Science Foundation, the Antorchas Foundation and the American Museum of Natural History.

<http://medicalxpress.com/news/2011-11-women-chin-abdomen-good-indicators.html>

Women's chin, abdomen are good indicators of excessive hair growth

Examining the chin and upper and lower abdomen is a reliable, minimally invasive way to screen for excessive hair growth in women, a key indicator of too much male hormone, researchers report.

"We wanted to find a way to identify this problem in women that was as non-intrusive and accurate as possible," said Dr. Ricardo Azziz, reproductive endocrinologist and President of Georgia Health Sciences University. "We believe this approach is approximately 80 percent accurate and will be less traumatic for women in many situations than the full body assessments currently used," said Azziz, corresponding author of the study published in the journal Fertility and Sterility.

In addition to cosmetic concerns, women with excessive hair growth, or hirsutism, are often overweight with menstrual dysfunction and diminished fertility related to problems with ovulation. Symptoms can begin in childhood. Hirsutism also is highly correlated with polycystic ovary syndrome, or PCOS, a major cause of infertility as well as a significant risk factor for diabetes and heart disease. PCOS is a subcategory of androgen excess or excess male hormone, the most common hormone disorder, which affects about 10 percent of women.

"If you do the math, at least half the women with excess hair growth will be at increased risk for insulin resistance, metabolic dysfunction, diabetes and heart disease. That is why this is such an important marker," Azziz said.

He calls hirsutism the single most defining feature of androgen excess disorder, such as PCOS. "Excessive hair growth strikes at the femininity of women. We are talking about terminal hairs that are harder, more pigmented and thicker than the usual soft hairs you see." In fact, Azziz and his colleagues have previously published studies indicating hirsutism is second to obesity in negatively impacting a woman's quality of life.

"You cover yourself up at the beach. You don't want your partner to see you nude. It can be very damaging to your psychosocial well-being," he said.

The most widely used assessment today is about 50 years old and includes nine body areas: the lip, chin, chest, upper and lower abdomen, upper arm, thigh and upper and lower back. Many women consider this full body check invasive and it can be unwieldy for scientists doing large epidemiologic studies, Azziz said.

For this study, Azziz examined 1,116 female patients at the University of Alabama at Birmingham from 1987-2002 and 835 female patients at Cedars-Sinai Medical Center in Los Angeles from 2003-09 with symptoms of androgen excess. Study authors note the method needs further evaluation, including whether it can be used to monitor success of hirsutism treatment. The hirsutism study is part of Azziz's ongoing research of the problems related to androgen excess and PCOS.

Diagnosis is a complex process that can include a history and physical exam, quantifying hair growth, measuring male hormone levels as well as an oral glucose tolerance test to determine the degree of insulin excess and diabetes risk, said Azziz's collaborator, Dr. Lawrence C. Layman, chief of the GHSU Section of Reproductive Endocrinology, Infertility and Genetics. It also requires ruling out syndromes or disorders with similar symptoms such as non-classic congenital adrenal hyperplasia, which Azziz's team helped differentiate. Current therapies, such as birth control pills to prevent androgen synthesis and the blood pressure medicine, spironolactone, a diuretic that also blocks androgen receptors, treat symptoms rather than causes, the researchers said.

To improve diagnosis and treatment, they along with Azziz's long time colleagues Dr. Yen-Hao Chen, biomedical scientist, and Saleh Heneidi, research associate, are expanding the GHSU Tissue Repository for Androgen-Related Disorders. In the past two decades, Azziz's team has collected more than 50,000 samples - including fat, blood, urine, plasma and DNA - from about 7,000 women. Having this variety of samples, particularly from the same woman, enables the scientists to better put together the pieces that contribute to the syndrome, Chen said.

"These women have been to a lot of doctors and a lot of clinics and they know that the medical knowledge out there is limited so they are willing to help further research in this field," Azziz said of the significant patient contributions.

Azziz is collaborating with scientists at Cedars-Sinai to identify the multiple genes responsible, which they suspect also have roles in insulin signaling, inflammation and androgen production. "We know that a significant portion of women with PCOS have an inherited defect of their insulin action which, along with other genetic defects, results in the syndrome," he said. "If we can find the genes that are abnormal, we may be able to find drugs to target those genes."

His GHSU team is also examining signaling abnormalities in fat - a determinant of insulin resistance - in PCOS patients. "Clearly fat in PCOS behaves differently than fat in healthy women of the same weight," Azziz said. They suspect the abnormal signals are partially to blame for the abnormal response to insulin. They also suspect the signaling abnormalities are good treatment targets. *Provided by Georgia Health Sciences University*

<http://www.bbc.co.uk/news/science-environment-15565654>

Early humans' route out of Africa 'confirmed'

A six-year effort to map the genetic patterns of humankind appears to confirm that early people first left Africa by crossing into Arabia.

Ancestors of modern people in Europe, Asia and Oceania migrated along a southern route, not a northern route through Egypt as some had supposed. The results from the Genographic Project are published in the journal *Molecular Biology and Evolution*. It suggests an important role for South Asia in the peopling of the world.

The ancestors of present-day non-African people left their ancestral homeland some 70,000 years ago.

The researchers found that Indian populations had more genetic diversity - which gives an indication of the age of a population - than either Europeans or East Asians. This supports the idea that pioneering settlers followed a southern coastal route as they populated east Asia and continued into Oceania.

"This suggests that other fields of research such as archaeology and anthropology should look for additional evidence on the migration route of early humans," said co-author Ajay Royyuru, senior manager at IBM's Computational Biology Center, which was involved in analysing the study data.

A route out of Africa via the Arabian Peninsula, along the southern coast of Asia, explained the observed patterns in genetic diversity much better than a route through Egypt's Sinai desert.

This agrees with other evidence showing that sea levels might have been low enough around 60-70,000 years ago for humans to cross from the horn of Africa into Arabia via the Bab-el-Mandeb straits in the Red Sea.

The latest findings are based on a new analytical method which exploits patterns of recombination in human genomes. Recombination is the process by which molecules of DNA are broken up and recombine to form new pairs. The scientists used these patterns of recombination to trace relationships between different present-day humans.

"Almost 99% of the genetic makeup of an individual are layers of genetic imprints of the individual's many lineages. Our challenge was whether it was even feasible to tease apart these lineages to understand the commonalities," said IBM researcher Laxmi Parida. "Through a determined approach of analytics and mathematical modelling, we undertook the intricate task of reconstructing the genetic history of a population. In doing so, we now have the tools to explore much more of the human genome."

Dr Spencer Wells, director of the Genographic Project, said such methods could provide "greater insights into the migratory history of our species". Nearly 500,000 individuals have participated in the project, making it one of the biggest surveys of human genetic variation ever conducted. The DNA was contributed by indigenous peoples and by members of the general public.

<http://www.sciencedaily.com/releases/2011/11/111102145736.htm>

Did Life Once Exist Below Red Planet's Surface? NASA Study of Clays Suggests Watery Mars Underground

ScienceDaily - A new NASA study suggests if life ever existed on Mars, the longest lasting habitats were most likely below the Red Planet's surface.

A new interpretation of years of mineral-mapping data, from more than 350 sites on Mars examined by European and NASA orbiters, suggests Martian environments with abundant liquid water on the surface existed only during short episodes. These episodes occurred toward the end of a period of hundreds of millions of years during which warm water interacted with subsurface rocks. This has implications about whether life existed on Mars and how the Martian atmosphere has changed.

"The types of clay minerals that formed in the shallow subsurface are all over Mars," said John Mustard, professor at Brown University in Providence, R.I. Mustard is a co-author of the study in the journal Nature. "The types that formed on the surface are found at very limited locations and are quite rare."

Discovery of clay minerals on Mars in 2005 indicated the planet once hosted warm, wet conditions. If those conditions existed on the surface for a long era, the planet would have needed a much thicker atmosphere than it has now to keep the water from evaporating or freezing. Researchers have sought evidence of processes that could cause a thick atmosphere to be lost over time.

This new study supports an alternative hypothesis that persistent warm water was confined to the subsurface and many erosional features were carved during brief periods when liquid water was stable at the surface.

"If surface habitats were short-term, that doesn't mean we should be glum about prospects for life on Mars, but it says something about what type of environment we might want to look in," said the report's lead author, Bethany Ehlmann, assistant professor at the California Institute of Technology, Pasadena, and scientist at NASA's Jet Propulsion Laboratory, also in Pasadena. "The most stable Mars habitats over long durations appear to have been in the subsurface. On Earth, underground geothermal environments have active ecosystems."

The discovery of clay minerals by the OMEGA spectrometer on the European Space Agency's Mars Express orbiter added to earlier evidence of liquid Martian water. Clays form from the interaction of water with rock. Different types of clay minerals result from different types of wet conditions.

During the past five years, researchers used OMEGA and NASA's Compact Reconnaissance Imaging Spectrometer, or CRISM, instrument on the Mars Reconnaissance Orbiter to identify clay minerals at thousands of locations on Mars. Clay minerals that form where the ratio of water interacting with rock is small generally retain the same chemical elements as those found in the original volcanic rocks later altered by the water.

The study interprets this to be the case for most terrains on Mars with iron and magnesium clays. In contrast, surface environments with higher ratios of water to rock can alter rocks further. Soluble elements are carried off by water, and different aluminum-rich clays form. Another clue is detection of a mineral called prehnite. It forms at temperatures above about 400 degrees Fahrenheit (about 200 degrees Celsius). These temperatures are typical of underground hydrothermal environments rather than surface waters.

"Our interpretation is a shift from thinking that the warm, wet environment was mostly at the surface to thinking it was mostly in the subsurface, with limited exceptions," said Scott Murchie of Johns Hopkins University Applied Physics Laboratory in Laurel, Md., a co-author of the report and principal investigator for CRISM.

One of the exceptions may be Gale Crater, the site targeted by NASA's Mars Science Laboratory mission. Launching this year, the mission's Curiosity rover will land and investigate layers that contain clay and sulfate

minerals. NASA's Mars Atmosphere and Volatile Evolution Mission, or MAVEN, in development for a 2013 launch, may provide evidence for or against this new interpretation of the Red Planet's environmental history. The report predicts MAVEN findings consistent with the atmosphere not having been thick enough to provide warm, wet surface conditions for a prolonged period.

JPL, a division of Caltech, manages the Mars Reconnaissance Orbiter for NASA's Science Mission Directorate in Washington. APL provided and operates CRISM. For more information about the Mars Reconnaissance Orbiter, visit: <http://www.nasa.gov/mro> and <http://mars.jpl.nasa.gov/mro>.

<http://medicalxpress.com/news/2011-11-measles-quickly.html>

Why measles spreads so quickly

Mayo Clinic researchers have discovered why measles, perhaps the most contagious viral disease in the world, spreads so quickly.

The virus emerges in the trachea of its host, provoking a cough that fills the air with particles ready to infect the next host. The findings may also help in the fight against ovarian, breast and lung cancers.

The findings, published online Nov. 2 in the journal *Nature*, give researchers insight into why some respiratory viruses spread more quickly and easily than others: They found the measles virus uses a protein (called nectin-4) in the host to infect and then leave from the strategic location of the throat.

Despite the development of a measles vaccine, the virus continues to affect more than 10 million children each year and kills about 120,000 worldwide. In recent years, the spread of the virus has increased due to lack of people being vaccinated, and measles is still a significant public health problem in the United States.

But why is the measles virus so much more contagious than other respiratory viruses?

"The measles virus has developed a strategy of diabolic elegance," says Roberto Cattaneo, Ph.D., principal investigator of the study and Mayo Clinic molecular biologist. "It first hijacks immune cells patrolling the lungs to get into the host. It then travels within other immune cells everywhere in the body.

"However, the infected immune cells deliver their cargo specifically to those cells that express the protein nectin-4, the new receptor. Remarkably, those cells are located in the trachea. Thus, the virus emerges from the host exactly where needed to facilitate contagion."

The researchers were also excited about another aspect of these findings. Nectin-4 is a biomarker of several types of cancer such as ovarian, breast and lung. Clinical trials are under way that use measles and other viruses to attack cancer - including current ovarian, glioma and myeloma clinical trials at Mayo Clinic.

Because measles actively targets nectin-4, measles-based cancer therapy may be more successful in patients whose cancer express nectin-4. Many researchers believe that modified viruses could be a less toxic alternative to chemotherapy and radiation. *Provided by Mayo Clinic*

<http://medicalxpress.com/news/2011-11-background-noise-affects-scores.html>

Study shows background noise affects test scores

A new study presented at the 162nd Meeting of the Acoustical Society of America shows that students testing scores are negatively affected by background noise, but not the noise you would expect.

Medical Xpress - The background noise affecting test scores is not loud classroom disruptions or traffic noise, but the humming that comes from school air conditioning and heating systems. While previous studies have shown that noise in the classroom is a distraction, they have always looked at more obvious noises, such as schools near airports. Lauren Ronsee from the U.S. Army Engineer Research and Development Center was interested in seeing how more subtle noise, such as the humming from the air conditioning and heating units, played a role in test scores. Researchers collected data last year from 58 empty second and fourth grade classrooms in an Iowa school district, measuring the volume. They then looked at the test scores from students in each classroom and what they found was that kids who spent most of their time in the louder classrooms produced lower test scores on standardized reading comprehension exams.

In another study, they repeated the volume collection in 67 empty classrooms in Nebraska public schools, but their results varied. Fifth grade students showed lower scores in louder rooms but the third grades saw no relationship. Those taking math exams showed no difference in scores.

The American National Standards Institute sets a recommendation for classroom background noise not to exceed 35 decibels. However, the researchers found that the Iowa classrooms had ranges of 36 to 50 decibels and the Nebraska schools were between 28 and 62 decibels. This research shows that in order for a student to perform their best on exams, the background noise needs to be below 28 decibels, or about the same as a whisper.

The researchers believe that this studies shows that more effort needs to be taken to enforce the American National Standards Institute's recommendations. They also suggest that new schools be built with air conditioning and heating systems that are quieter in order to provide an optimal learning environment for children. *More information: Abstract online: <http://asa.aip.org ... 11/asa9.html>*

<http://www.physorg.com/news/2011-11-brain-pupil-constriction.html>

Brain control? Shining light on pupil constriction

A doctor shines a bright light into an unconscious patient's eye to check for brain death. If the pupil constricts, the brain is OK, because the brain controls the pupil. Or does it?

PhysOrg.com - You've seen it on television: A doctor shines a bright light into an unconscious patient's eye to check for brain death. If the pupil constricts, the brain is OK, because in mammals, the brain controls the pupil. Or does it? Now, researchers at Johns Hopkins have discovered that in most mammals, in fact in most vertebrates, the pupil can constrict without any input from the brain. Their work, which also describes for the first time the molecular mechanism underlying this process, appears in the Nov. 3 issue of Nature.

"It was established more than 40 years ago that animals like amphibians and fish have photosensitive irises and don't necessarily require the brain for the pupillary light reflex, whereas it was thought that mammals generally required brain circuitry," says King-Wai Yau, Ph.D., professor of neuroscience and ophthalmology at the Johns Hopkins University School of Medicine and member of the Institute for Basic Biomedical Sciences Center for Sensory Biology. "But in neither case did anyone know what the molecular switch was, and now we have found that it's the pigment melanopsin."

The research team examined isolated irises from a wide range of mammals by attaching a tiny meter that measures the force of the sphincter muscle that constricts the pupil. They then shined a bright light onto this muscle and measured any contraction. Irises from nocturnal animals including mouse, rat, hamster, dog, cat, rabbit and the Nile grass rat all showed responses to light. Irises from diurnal animals including guinea pig, ground squirrel and pig did not, nor did those from rhesus monkey, marmoset, owl monkey and bush baby, even though the owl monkey and bush baby are nocturnal.

"Most non-primate mammals are considered nocturnal or crepuscular - active at dawn and dusk - including those, like dogs, that have been domesticated and have picked up human circadian rhythms," says Yau. "We don't really know why primates, including us, as well as other daytime functioning animals don't have this ability." According to Yau, the eyes of nocturnal animals, because they function in the dark, contain more cells that are sensitive to low light and exposure to bright light could cause eye damage. Perhaps, he suggests, the built-in pupil reflex is a good way to protect the eye.

"So of course we wanted to know what pigment molecules are involved in triggering pupil constriction," says Yau. Having previously genetically engineered mice to lack melanopsin, the team first tested the pupillary light reflex on irises from these mice. "That was a really exciting result—they didn't respond to the light," says Tian Xue, a research associate with Yau. They also tested mice engineered to lack other light-capturing pigments, but all of them responded normally, suggesting that only melanopsin is required for the local pupil reflex. Using mouse genetics, the team then continued to try to identify other proteins that work with melanopsin to cause the pupil to contract in response to light.

Because melanopsin is closely related to the pigment responsible for capturing light in fly eyes, and that molecular pathway has been well studied, Yau's team hypothesized that the mammalian counterparts to these fly molecules might be what works with melanopsin. So they tested mice engineered to lack some of these molecules. They found that irises from mice lacking the PLC enzyme were unresponsive to light, showing that PLC also is involved in this reflex.

There still are a lot of things we don't know that we would like to study," says Yau. "Now that we know what captures the light and starts the local reflex, we would like to know what proteins in the muscle trigger the actual contraction." *Provided by Johns Hopkins University*

<http://www.bbc.co.uk/news/health-15561501>

English-style diet 'could save 4,000' in rest of UK

Eating like the English could save 4,000 lives a year in Scotland, Wales and Northern Ireland, a study claims.

By Helen Briggs Health editor, BBC News website

People in England eat more fruit and vegetables and less salt and fat, reducing heart disease and some cancers, say Oxford University experts. A tax on fatty and salty foods and subsidies on fruit and vegetables could help close the diet divide, they add. The British Heart Foundation says the study shows inequalities in the nations that must be addressed by authorities.

Death rates for heart disease and cancer are higher in Scotland, Wales and Northern Ireland than in England, according to official figures. Diet is known to be an important factor. Last year researchers estimated that more than 30,000 lives a year would be saved if everyone in the UK followed dietary guidelines on fat, salt, fibre, and fruit and vegetables. Now, the same experts - from the Department of Public Health at the University of Oxford - have turned their attention to differences within the UK.

They looked at whether deaths from heart disease, stroke and 10 cancers linked with poor diet could be prevented in Scotland, Wales and Northern Ireland, if everyone switched to the typical English diet. They say the diet in England is far from perfect - but should be achievable in other UK countries. Over the three years studied there were nearly 22,000 excess deaths in total. Scotland had 15,719, Wales 3,723 and Northern Ireland 2,329.

Hamburger tax

Lead researcher Dr Peter Scarborough of the Health Promotion Research Group said: "The chief dietary factor that is driving this mortality gap is fruit and vegetables. "Consumption of fruit and vegetables in Scotland is around 12% lower than in England, and consumption in Northern Ireland is about 20% lower than in England. Consumption levels in Wales are similar. "Other important factors are salt and saturated fat consumption, which are lower in England than in Wales, Scotland or Northern Ireland."

The researchers believe one way to tackle the "mortality gap" is to bring in food taxes. Denmark recently introduced a tax on foods high in saturated fat, while other countries are toying with the idea of taxing fizzy drinks or high-calorie foods.

Dr Scarborough told the BBC that while the study did not consider the effectiveness of policies and interventions, the area should be investigated. He said: "Junk food taxes and subsidies of fruit and veg could be a very important tool in addressing health inequalities in the UK." The researchers say they used the English diet as their model not because it is particularly healthy, but because it is regarded as an achievable goal.

Victoria Taylor, senior dietician at the British Heart Foundation, said: "This research isn't about bragging rights to the English or tit-for-tat arguments about how healthy our traditional dishes might be.

"This is a useful exercise in comparing influential differences in diet across the UK, namely calorie intake and fruit and veg consumption. However, saying the rest of the UK should follow England's lead to cut heart deaths isn't a foolproof solution; a quarter of English adults are obese and only 30% eat their five-a-day.

"The findings have thrown up some clear inequalities in the four nations and our governments must do everything they can to create environments that help people make healthy choices."

The research is published in the medical journal BMJ Open.

http://www.eurekalert.org/pub_releases/2011-11/bc-xmt110211.php

X marks the spot - TBL1X gene involved in autism spectrum disorder

New research used genome wide association study data to find a variation in the gene for transducin β -like 1X-linked which is associated with increased risk of ASD in boys

Autism Spectrum Disorder (ASD) affects about 1 in 100 children resulting in a range of problems in language, communication and understanding other people's emotional cues, all of which can lead to difficulties in social situations. Boys are three to four more times as likely to be affected as girls and consequently it has been suggested that the genes involved in this disorder may be linked to the X chromosome. New research published in BioMed Central's open access journal Molecular Autism used genome wide association study (GWAS) data to find a variation in the gene for transducin β -like 1X-linked (TBL1X) which is associated with increased risk of ASD in boys.

A team of researchers across America combined three sets of genomic data incorporating over 3000 affected children and their family members or non-related case control individuals. The GWAS study compared single nucleotide polymorphisms (SNP) on the X chromosomes of the children with ASD to the control groups, and found differences within the genes for Duchenne muscular dystrophy (DMD), IL1RAPL2 (involved in inflammation), and in TBL1X. TBL1X is part of the Wnt-signaling pathway, which is in turn part of the complex mechanism controlling embryonic neurological development and the maintenance of brain function in adults.

Prof Eden Martin from the Hussman Institute for Human Genomics, who lead the multi-centre team explained, "The SNP in TBL1X is associated with an increase in risk for ASD of about 15%. This could reflect either an unidentified rare mutation (or mutations), which has large impact, or a more common change with a more subtle effect, on the development of ASD. Further study of TBL1X will help us to pinpoint the DNA changes involved and help us to understand exactly how these changes and the Wnt-signaling pathway is involved in ASD."

1. An X-chromosome-wide association study in autism families identifies TBLIX as a novel autism spectrum disorder candidate gene in males Ren-Hua Chung, Deqiong Ma, Kai Wang, Dale J Hedges, James M Jaworski, John R Gilbert, Michael L Cuccaro, Harry H Wright, Ruth K Abramson, Ioanna Konidari, Patrice L Whitehead, Gerard D Schellenberg, Hakon Hakonarson, Jonathan L Haines, Margaret A Pericak-Vance and Eden R Martin *Molecular Autism* (in press)

http://www.eurekalert.org/pub_releases/2011-11/ind-ets110311.php

Erasing the signs of aging in cells is now a reality

Inserm's AVENIR team has recently succeeded in rejuvenating cells from elderly donors

Inserm's AVENIR "Genomic plasticity and aging" team, directed by Jean-Marc Lemaître, Inserm researcher at the Functional Genomics Institute (Inserm/CNRS/Université de Montpellier 1 and 2), has recently succeeded in rejuvenating cells from elderly donors (aged over 100). These old cells were reprogrammed in vitro to induced pluripotent stem cells (iPSC) and to rejuvenated and human embryonic stem cells (hESC): cells of all types can again be differentiated after this genuine "rejuvenation" therapy. The results represent significant progress for research into iPSC cells and a further step forwards for regenerative medicine.

The results are published in the *Genes & Development* Journal dated 1 November 2011.

Human embryonic stem cells (hESC) are undifferentiated multiple-function cells. They can divide and form all types of differentiated adult cells in the body (neurones, cardiac cells, skin cells, liver cells, etc...)

Since 2007, a handful of research teams across the world have been capable of reprogramming human adult cells into induced pluripotent cells (iPSC), which have similar characteristics and potential to human embryonic stem cells (hESC). This kind of reprogramming makes it possible to reform all human cell types without the ethical restrictions related to using embryonic stem cells.

Until now, research results demonstrated that senescence (the final stage of cellular aging) was an obstacle blocking the use of this technique for therapeutic applications in elderly patients.

Today, Inserm researcher Jean-Marc Lemaître and his team have overcome this obstacle. The researchers have successfully rejuvenated cells from elderly donors, some over 100 years old, thus demonstrating the reversibility of the cellular aging process.

To achieve this, they used an adapted strategy that consisted of reprogramming cells using a specific "cocktail" of six genetic factors, while erasing signs of aging. The researchers proved that the iPSC cells thus obtained then had the capacity to reform all types of human cells. They have the physiological characteristics of "young" cells, both from the perspective of their proliferative capacity and their cellular metabolisms.

A cocktail of six genetic factors...

Researchers first multiplied skin cells (fibroblasts) from a 74 year-old donor to obtain the senescence characterized by the end of cellular proliferation. They then completed the in vitro reprogramming of the cells. In this study, Jean-Marc Lemaître and his team firstly confirmed that this was not possible using the batch of four genetic factors (OCT4, SOX2, C MYC and KLF4) traditionally used. They then added two additional factors (NANOG and LIN28) that made it possible to overcome this barrier.

Using this new "cocktail" of six factors, the senescent cells, programmed into functional iPSC cells, re-acquired the characteristics of embryonic pluripotent stem cells. In particular, they recovered their capacity for self-renewal and their former differentiation potential, and do not preserve any traces of previous aging.

To check the "rejuvenated" characteristics of these cells, the researchers tested the reverse process. The rejuvenated iPSC cells were again differentiated to adult cells and compared to the original old cells, as well as to those obtained using human embryonic pluripotent stem cells (hESC). "Signs of aging were erased and the iPSCs obtained can produce functional cells, of any type, with an increased proliferation capacity and longevity," explains Jean-Marc Lemaître who directs the Inserm AVENIR team.

...tested on cells taken from donors over the age of 100.

The results obtained led the research team to test the cocktail on even older cells taken from donors of 92, 94 and 96, and even up to 101 years old. "Our strategy worked on cells taken from donors in their 100s. The age of cells is definitely not a reprogramming barrier." He concluded. "This research paves the way for the therapeutic use of iPS, insofar as an ideal source of adult cells is provided, which are tolerated by the immune system and can repair organs or tissues in elderly patients." adds the researcher.

Inserm Transfert filed a patent request for this research.

Jean-Marc Lemaître took advantage of the Avenir programme in 2006. This programme was created in 2001 by Inserm and provides a platform for young researchers, who have obtained their PhD in science, to set up and coordinate a team within an existing research structure. In 2009, Inserm and CNRS merged their respective programmes aimed at young researchers, and from that date on they have launched a joint call for proposals: Atip-Avenir. *Genes & Development*, 1er Novembre 2011 Vol. 25, No. 21, doi:10.1101/gad.173922.111

Alternate ending - living on without telomerase

Scientists of the German Cancer Research Center have discovered an alternative mechanism for the extension of the telomere repeat sequence by DNA repair enzymes.

The ends of the chromosomes, the telomeres, are repetitive DNA sequences that shorten every time a cell divides during the process of duplicating its genome. Once the telomeres become very short the cell stops dividing. Thus, telomeres work like a cellular clock that keeps an eye on the number of cell divisions. And once the cell's time is over it can no longer divide. Circumventing this control mechanism is crucial for tumor cells in order to proliferate without limits. In the majority of tumors this is accomplished by reactivating telomerase, an enzyme that normally extends the telomeres only in embryonic cells, and thus resets the cellular clock during development. However, a 10-15% fraction of tumors keeps on dividing without telomerase by making use of what is called the ALT-mechanism for "Alternative Lengthening of Telomeres". The hallmark of ALT cancer cells is a special type of complexes of promyelocytic leukemia (PML) protein at the telomeres that are termed ALT-associated PML nuclear bodies or APBs.

ALT-tumors can be identified by the presence of APBs on fluorescence microscopy images since normal cells do not have these structures. However, the function of APBs has remained mysterious. In a recent study, Inn Chung and Karsten Rippe from the German Cancer Research Center together with Heinrich Leonhardt from the LMU in Munich applied a novel approach to study APBs. They succeeded in artificially making APBs in living cells by tethering PML and other APB proteins to the telomeres. In this manner they could not only trace the assembly of APBs but were able to investigate what happens after APB formation. They could show that the de novo formed APBs induced the extension of the telomere repeat sequence by a DNA repair synthesis mechanism. This demonstrates for the first time that APBs have an important function for the alternative telomere lengthening mechanism, and suggests that disrupting APBs would stop proliferation of ALT-positive tumor cells once their telomeres become too short. This makes APBs a promising new target of cancer cells, in which the ALT mechanism is active.

Publication: Chung, I., Leonhardt, H. & Rippe, K. (2011). De novo assembly of a PML nuclear subcompartment occurs through multiple pathways and induces telomere elongation. J. Cell Sci., doi: 10.1242/jcs.084681.

<http://www.physorg.com/news/2011-11-explosive-composite-based-nanoparticles-dna.html>

Explosive composite based on nanoparticles and DNA could be an energy source for embedded microsystems

A solid explosive with an energy density equivalent to that of nitroglycerine

A solid explosive with an energy density equivalent to that of nitroglycerine: this is the composite material produced by researchers at the Laboratoire d'Analyse et d'Architecture des Systemes (CNRS) in Toulouse, France, using an innovative production process that brings nanoparticles into contact with strands of DNA. These strands then "assemble" the various kinds of nanoparticles used. The released energy and ignition temperature of the new explosive are among the best ever described in the literature. The explosive could thus be used as an energy source to power embedded systems, both in space and in the environment. This innovative material is the subject of a paper published online in the journal *Advanced Functional Materials*.

Nanoparticles of aluminium and copper oxide make up the two basic ingredients of the composite material. Although the idea of coupling aluminium with copper oxide to produce energy is not new (they were once used to weld railway tracks), this is the first time that DNA strands have been used to assemble them. So why use DNA? Two complementary DNA strands (i.e. whose molecules are able to recognize each other) self-assemble into a double helix and then remain firmly bound together, just as they are in every cell of our body. The researchers made use of these 'sticky' properties. They separately grafted strands of DNA onto nanoscopic beads of aluminium and of copper oxide before mixing together the two types of nanoparticles coated with DNA strands. As a result, the complementary strands on each type of nanoparticle bind, turning the original aluminium and copper oxide powder into a compact, solid material which spontaneously ignites when heated to 410 °C (one of the lowest spontaneous ignition temperatures hitherto described in the literature).

In addition to its low ignition temperature, this composite also offers the advantage of having a high energy density, similar to nitroglycerine: for the same quantity of material, it produces considerably more heat than aluminium and copper oxide taken separately, where a significant part of the energy is not released. In contrast, by using nanoparticles, with their large active surfaces, the researchers were able to approach the maximum theoretical energy for this exothermic chemical reaction.

The high energy density of this composite makes it an ideal fuel for nanosatellites, which weigh a handful of kilograms and are increasingly used. Such satellites are too light to be equipped with a conventional propulsion

system once in orbit. However, a few hundred grams of this composite would give them sufficient energy to adjust their trajectory and orientation.

The composite could also have a host of terrestrial applications: ignitors for gas in internal combustion engines or for fuel in aircraft and rocket nozzles, miniature detonators, on-site welding tools, etc. Once its heat is turned into electrical energy, the composite could also be used as a back-up source for microsystems (such as pollution detectors scattered through the environment).

More information: High Energy Al/CuO nanocomposites obtained by DNA-directed assembly. F. Séverac, et al, Adv. Funct. Mater., online October 18 2011. Provided by CNRS

<http://medicalxpress.com/news/2011-11-embryonic-pancreatic-cancer.html>

Embryonic signal drives pancreatic cancer and offers a way to kill it

Researchers have evidence to suggest there is a way to kill off pancreatic cancer stem cells

Pancreatic cancer is a particularly challenging one to beat; it has a tendency to spread and harbors cancer stem cells that stubbornly resist conventional approaches to therapy. Now, researchers reporting in the November issue of Cell Stem Cell, a Cell Press publication, have evidence to suggest there is a way to kill off those cancer stem cells. The target is a self-renewal pathway known for its role not in cancer but in embryonic stem cells.

"I don't think the cancer stem cells have any direct link to embryonic development, rather they are using this developmental pathway for their uncontrolled self-renewal capacity," said Christopher Heeschen of the Spanish National Cancer Research Centre in Madrid. "This pathway is completely inactive in adult tissue. We've checked many tissues and there is zero – no detectable expression at all."

The so-called Nodal/Activin pathway's embryonic ties and absence from other tissues present a real opportunity. It suggests you could target the molecular pathway without harming other adult cells. Heeschen's team has now shown that approach to therapy does seem to work in mice.

They first demonstrated the important role of the Nodal/Activin pathway in cancer stem cells derived from human pancreatic cancer. When that signal was blocked, normally resistant pancreatic cancer stem cells became sensitive to chemotherapy. The researchers then moved on to experiments in mice with established tumors seeded from human cancer cells. Treatment of those animals with the pathway inhibitor plus standard chemotherapy eliminated those stem cells. "The dual combination therapy worked strikingly well," Heeschen said. "The mice responded with 100 percent survival after 100 days." That's compared to mice not receiving the therapy, which bore large tumors and died within 40 days of implantation.

That two-part treatment wasn't enough to tackle pancreatic cancer when intact tumor tissue was implanted into mice as opposed to just cancer cells, the researchers found. Heeschen says that's because those cells were nestled within a supportive "stroma." That protective tissue delivered the Activin signal and prevented the drug combination from reaching the cells.

To get around that, Heeschen and his colleagues added a third ingredient to therapy, an inhibitor intended to target the stroma. The three-pronged approach translated into long-term, progression-free survival for the mice.

Interestingly, Heeschen says the animals' tumors didn't show signs of shrinking even as they were defeated. "They were more or less dead tissue. They were senescent with no cancer stem cells – just sitting there," he said.

Those tissues apparently had no ability to form new tumors. The findings suggest that tumor regression isn't always the key thing to look for. It also shows that drugs designed to target cancer stem cells alone are promising, but only in combination with other drugs.

"The concept that you can hit cancer stem cells and tumors will melt away must be abandoned," Heeschen said. "You have to treat the entire cancer - the stroma, cancer stem cells and differentiated cells - as a complex."

Heeschen says there are hints that this embryonic pathway might have important roles in other forms of cancer, including breast, lung and colorectal cancers. That's something they will now test in further studies.

Provided by Cell Press

<http://www.wired.com/wiredscience/2011/11/sperm-whales/>

Sperm Whales Really Do Learn From Each Other

Sperm whales, Earth's biggest-brained animals, live in far-flung clans with lifestyles so different and vocalizations so complex that it's natural to think they have culture.

By Brandon Keim Email Author

But is that really true? Might sperm whales simply be following genetic instructions? Could their "culture" really be a set of instinctive, mechanical imperatives?

Researchers led by Hal Whitehead of Dalhousie University and Luke Rendell of Scotland's St. Andrews University, two of the world's foremost sperm whale biologists, have asked just this question.

Their findings: Yes, sperm whale culture really is culture. And how.

“As far as we know, these are the largest cultures on Earth, aside from human ethnicities,” said Whitehead. “They may have thousands or tens of thousands of members, covering thousands of kilometers of ocean.”

In a study published Oct. 21 in *Behavior Genetics*, Whitehead and Rendell analyzed sound recordings and skin samples from 194 sperm whales in the southwest Pacific Ocean.

The whales belonged to three “vocal clans,” each possessing a distinctively different repertoire of the Morse code-like clicks used by sperm whales to communicate. Were these dialects biologically determined, the whales would have overlapped genetically as well as vocally - but that’s not what the researchers found.

Instead, whales from different clans are often genetically similar. They’re not identical, but there’s no sign of genetic differences large enough to explain clan differences. These aren’t just vocal: Each clan also differs in hunting patterns, reproductive rates and parenting habits.

“If the differences were genetic, this would make the differences more traditionally biological. We’d have two different subspecies,” said Whitehead. “It’s culture, not genetics.”

The researchers also looked at whether geography might play a role, with each clan responding to local environments. But that doesn’t seem to be a factor: Clans can occupy vast and overlapping swaths of ocean, not a little unlike indigenous human tribes in pre-colonial North America. “This is like a situation that happens more rarely with humans, where you have several ethnic groups living in the same area but maintaining their identity,” Whitehead said.

In future research, Whitehead and Rendell hope to learn how sperm whale culture passes from generation to generation and between families.

The findings could influence conservation efforts, highlighting the importance of preserving threatened whale cultures. More fundamentally, they affect how people think of cetaceans - not just sperm whales, which are fortunate enough to have been studied by Whitehead and collaborators for decades, but all those species that remain unknown. “If differences are cultural, we’re getting into the border between biology and anthropology,” said Whitehead. “We’re infringing on some of the traits that some people think are unique to humans.”

*Citation: “Can Genetic Differences Explain Vocal Dialect Variation in Sperm Whales, *Physeter macrocephalus*?” By Luke Rendell, Sarah L. Mesnick, Merel L. Dalebout, Jessica Burtenshaw and Hal Whitehead. *Behavior Genetics*, Oct. 21, 2011*

http://www.sciencenews.org/view/generic/id/335845/title/Headache_tree_is_a_pain_in_the_brain

Headache tree is a pain in the brain

Bay laurel swells cranial blood vessels

By Rachel Ehrenberg

One whiff of a plant known as the headache tree can spur intense, excruciating pain - and now scientists know why. An ingredient in the tree sets off a chain of events that eventually amps up blood flow to the brain’s outer membrane.

Other headache triggers, such as chlorine, cigarette smoke and formaldehyde, interact with some of the same cellular machinery, suggesting they all work via the same pain-inducing mechanism.



Scientists have deciphered how an ingredient in the bay laurel tree (*Umbellularia californica*) triggers headaches in some people. Credit: Dlanglois/Wikimedia Commons

In the new study, an international group of researchers extracted the plant compound umbellulone from dried bay laurel leaves and then exposed various mouse and rat cells to the compound. Umbellulone tickles the same cellular detector that responds to painfully cold stimuli and the sinus-clearing scent of wasabi and mustard oil, the researchers report online October 27 in *Brain*. Stimulating this chemical detector ultimately triggers the release of a particular protein implicated in migraine headaches, the researchers found. This protein prompts blood vessels to swell, and scientists think this swelling puts pressure on the skull and nerves, causing pain.

The new research is solid, says neuroscientist Peter Goadsby, director of the headache center at the University of California, San Francisco. Other irritants linked to headaches interact with the same chemical detector, and it may be a good target for therapy, Goadsby says.

The scent of the bay laurel tree, *Umbellularia californica*, had been anecdotally implicated as a headache trigger, but it took a self-experimenting headache-sufferer to bring the plant to the attention of researchers in the Headache Center at the University of Florence. Pierangelo Geppetti, who led the study, heard from a friend about a man who was trimming trees on his property and suddenly experienced a cold sensation in his left

nostril and then excruciating pain around his left eye. In his youth, the man had regularly gotten cluster headaches, which are one-sided, intense bouts of exceptional pain that often recur in people who suffer from them.

Unlike a full-bore cluster headache, the man's symptoms quickly faded, and he forgot about the episode. But a few months later when he was again working with bay laurel, the headache struck again. This prompted him to experiment, intentionally sniffing the crushed leaves of the tree. The intense pain resumed and not long after, Geppetti heard the headache story from their mutual friend. Intrigued, he began investigating the chemical compounds that might be responsible.

http://www.eurekalert.org/pub_releases/2011-11/eic-hdo110211.php

Hubble directly observes the disc around a black hole

An international team of astronomers has used a new technique to study the bright disc of matter surrounding a faraway black hole.

Using the NASA/ESA Hubble Space Telescope, combined with the gravitational lensing effect of stars in a distant galaxy, the team measured the disc's size and studied the colours (and hence the temperatures) of different parts of the disc. These observations show a level of precision equivalent to spotting individual grains of sand on the surface of the Moon.

While black holes themselves are invisible, the forces they unleash cause some of the brightest phenomena in the Universe. Quasars - short for quasi-stellar objects - are glowing discs of matter that orbit supermassive black holes, heating up and emitting extremely bright radiation as they do so.

"A quasar accretion disc has a typical size of a few light-days, or around 100 billion kilometres across, but they lie billions of light-years away. This means their apparent size when viewed from Earth is so small that we will probably never have a telescope powerful enough to see their structure directly," explains Jose Muñoz, the lead scientist in this study.

Until now, the minute apparent size of quasars has meant that most of our knowledge of their inner structure has been based on theoretical extrapolations, rather than direct observations.

The team therefore used an innovative method to study the quasar: using the stars in an intervening galaxy as a scanning microscope to probe features in the quasar's disc that would otherwise be far too small to see. As these stars move across the light from the quasar, gravitational effects amplify the light from different parts of the quasar, giving detailed colour information for a line that crosses through the accretion disc.

The team observed a group of distant quasars that are gravitationally lensed by the chance alignment of other galaxies in the foreground, producing several images of the quasar.

They spotted subtle differences in colour between the images, and changes in colour over the time the observations were carried out. Part of these colour differences are caused by the properties of dust in the intervening galaxies: the light coming from each one of the lensed images has followed a different path through the galaxy, so that the various colours encapsulate information about the material within the galaxy. Measuring the way and extent to which the dust within the galaxies blocks light (known to astronomers as the extinction law) at such distances is itself an important result in the study.



This picture shows a quasar that has been gravitationally lensed by a galaxy in the foreground, which can be seen as a faint shape around the two bright images of the quasar. Observations of one of the images show variations in color over time. This is caused by stars within the lens galaxy passing through the path of the light from the quasar, magnifying the light from different parts of the quasar's accretion disc as they move. This has allowed a team of scientists to reconstruct the color and temperature profile of the accretion disc with unprecedented precision. The level of detail involved is equivalent to being able to study individual grains of sand on the surface of the Moon while standing on Earth. NASA, ESA and J.A. Muñoz University of Valencia

For one of the quasars they studied, though, there were clear signs that stars in the intervening galaxy were passing through the path of the light from the quasar. Just as the gravitational effect due to the whole intervening galaxy can bend and amplify the quasar's light, so can that of the stars within the intervening galaxy subtly bend and amplify the light from different parts of the accretion disc as they pass through the path of the quasar's light.

By recording the variation in colour, the team were able to reconstruct the colour profile across the accretion disc. This is important because the temperature of an accretion disc increases the closer it is to the black hole,

and the colours emitted by the hot matter get bluer the hotter they are. This allowed the team to measure the diameter of the disc of hot matter, and plot how hot it is at different distances from the centre. They found that the disc is between four and eleven light-days across (approximately 100 to 300 billion kilometres). While this measurement shows large uncertainties, it is still a remarkably accurate measurement for a small object at such a great distance, and the method holds great potential for increased accuracy in the future.

"This result is very relevant because it implies we are now able to obtain observational data on the structure of these systems, rather than relying on theory alone," says Muñoz. "Quasars' physical properties are not yet well understood. This new ability to obtain observational measurements is therefore opening a new window to help understand the nature of these objects."

Notes The Hubble Space Telescope is a project of international cooperation between ESA and NASA.

The study, entitled "A study of gravitational lens chromaticity with the Hubble Space Telescope", will appear in the December 1 issue of the Astrophysical Journal. The international team of astronomers consists of: J. A. Muñoz (University of Valencia, Spain), E. Mediavilla (Instituto de Astrofísica de Canarias, Spain), C. S. Kochanek (Ohio State University, USA), E. E. Falco (Harvard-Smithsonian Center for Astrophysics, USA) and A. M. Mosquera (University of Valencia and Ohio State University).

http://www.eurekalert.org/pub_releases/2011-11/uof-mrm110311.php

Medical researchers make important research link between active ingredient in saffron and MS

Medical researchers at the University of Alberta have discovered that an active ingredient in the Persian spice saffron may be a potential treatment for diseases involving neuroinflammation, such as multiple sclerosis.

Chris Power and a team of researchers in the Faculty of Medicine & Dentistry recently published their findings in the peer-reviewed publication, The Journal of Immunology. "We found there is a compound in saffron, known as crocin, that exerts a protective effect in brain cell cultures and other models of MS. It prevented damage to cells that make myelin in the brain," Power said. "Myelin is insulation around nerves. MS is characterized by inflamed brain cells that have lost this protective insulation, which ultimately leads to neurodegeneration." Power noted they are not close to a clinical trial stage yet, but the finding is still exciting.

It has been known in the research community for years that crocin protected neurons in certain situations, but Power and his team wanted to delve further into this area. His team discovered that inflammation and a specific type of cell stress are closely linked and lead to neurodegeneration and inflammation which cause cells to lose their protective coating – a process known as demyelination. In experiments conducted by Power and his colleagues, the use of crocin suppressed both inflammation and this specific type of cell stress, resulting in decreased neurological impairment in lab models and cell cultures with MS.

"There are still many questions to be answered about how crocin exerts these neuroprotective effects, but this research highlights a potential treatment role for crocin in diseases involving chronic neuroinflammation – something that had not been recognized until now," says Power. He explained the research demonstrates a new mechanism in MS, provides new potential drug targets in the future, and helps explain why physicians see inflammation in MS. The team's research also revealed that this specific type of cell stress, called the unfolded protein response, may be caused by an ancient virus that was introduced into the DNA of early humans.

This particular cell stress is found at high levels in MS brain lesions. "We all have this ancient virus in our DNA, but for some reason it is excessively turned on in MS," says Power. "We are doing more research investigating this link." Power has been investigating this specific area for six to seven years.

His research is funded by the MS Society of Canada and the federal government through the Canada Research Chair program.

http://www.eurekalert.org/pub_releases/2011-11/uol-bpd110411.php

Brain parasite directly alters brain chemistry

A research group has shown that infection by the brain parasite Toxoplasma gondii directly affects the production of dopamine

A research group from the University of Leeds has shown that infection by the brain parasite Toxoplasma gondii, found in 10-20 per cent of the UK's population, directly affects the production of dopamine, a key chemical messenger in the brain. Their findings are the first to demonstrate that a parasite found in the brain of mammals can affect dopamine levels.

Whilst the work has been carried out with rodents, lead investigator Dr Glenn McConkey of the University's Faculty of Biological Sciences, believes that the findings could ultimately shed new light on treating human neurological disorders that are dopamine-related such as schizophrenia, attention deficit hyperactivity disorder, and Parkinson's disease.

This research may explain how these parasites, remarkably, manipulate rodents' behaviour for their own advantage. Infected mice and rats lose their innate fear of cats, increasing the chances of being caught and eaten, which enables the parasite to return to its main host to complete its life cycle. In this study, funded by the Stanley Medical Research Institute and Dunhill Medical Trust, the research team found that the parasite causes production and release of many times the normal amount of dopamine in infected brain cells.

Dopamine is a natural chemical which relays messages in the brain controlling aspects of movement, cognition and behaviour. It helps control the brain's reward and pleasure centres and regulates emotional responses such as fear. The presence of a certain kind of dopamine receptor is also associated with sensation-seeking, whereas dopamine deficiency in humans results in Parkinson's disease.

These findings build on earlier studies in which Dr McConkey's group found that the parasite actually encodes the enzyme for producing dopamine in its genome. "Based on these analyses, it was clear that *T. gondii* can orchestrate a significant increase in dopamine production in neural cells," says Dr McConkey.

"Humans are accidental hosts to *T. gondii* and the parasite could end up anywhere in the brain, so human symptoms of toxoplasmosis infection may depend on where parasite ends up. This may explain the observed statistical link between incidences of schizophrenia and toxoplasmosis infection."

Dr McConkey says his next experiments will investigate how the parasite enzyme triggers dopamine production and how this may change behaviour.

<http://medicalxpress.com/news/2011-11-laser-treatment-brown-eyes-blue.html>

Laser treatment can make your brown eyes blue

Just like the old Crystal Gayle song, a new laser technology could soon allow you to turn those boring brown eyes of your to a rich and beautiful blue.

But you better make sure that blue eyes are what you really want because there is no reversing this surgery.

Dr. Gregg Homer from Stroma Medical in Laguna Brach, California has developed a new treatment known as Lumineyes. Homer has been working on the treatment for the last 10 years and submitted a patent for the idea in 2005.

People with brown eyes have a pigment known as melanin in the front of their irises. People with blue eyes, or the recessive traits, have this brown melanin but only in the back of the iris. It is this lack of pigment that creates the blue color. In Dr. Homer's procedure, which only takes about 20 seconds, a laser is used to remove the melanin from the top layer of the iris. Within a few weeks, the blue eye color emerges.

But don't start making phone calls and getting in line to have your eye color changed just yet. This procedure has only had limited testing on humans and the company is currently seeking funding to complete human trials. It is the hope of Dr. Homer that the procedure will be available outside the U.S. within the next 18 months and U.S. residents could see it becoming available within the next three years.

With so many people turning to cosmetic contact lenses to change the color of their eyes, this new procedure would offer a permanent alternative. Dark eyes are much more common than blue eyes, with about 80 percent of the population having the darker pigment. Stroma Medical has conducted two different surveys that show 17 percent of these dark-eyed people would choose the permanent color change if it was safe and effective.

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<http://medicalxpress.com/news/2011-11-china-fake-medicine-racket.html>

China breaks up fake medicine racket

China said Friday it had busted a gang that produced and sold fake medicine - some made of animal feed -- arresting 114 suspects and seizing more than 65 million counterfeit tablets.

China has frequently been hit by fake drug scandals despite government pledges to improve supervision of the industry, triggering growing public outrage over lax controls and official corruption.

The Ministry of Public Security said in a statement that around 1,000 police officers raided 117 dens and pharmacies that produced and sold fake drugs. The raids were the result of a four-month investigation during which police discovered that the gang repackaged expired pharmaceuticals, or used dangerous ingredients such as animal feed and chemical pigments to make tablets. "In order to make the fake drugs similar to the real medicine in colour, weight and other senses, some even added iron powder and diazepam (used to treat anxiety disorders) into their products... which caused huge harm to patients," it said.

The statement did not mention whether anyone had died or fallen ill after taking the counterfeit medicines or when the raids occurred. Most of the fake drugs were sold to clinics and pharmacies outside city centres or in the countryside, and the sellers used newspapers, magazines and particularly the Internet for promotion, it said.

The case is the latest in a string of food and drug safety scandals to hit the nation.

In 2007, Zheng Xiaoyu, former head of the State Food and Drug Administration, was executed for accepting \$850,000 in bribes in exchange for granting approval for hundreds of medicines, some of which were later found to be dangerous. The case triggered governmental pledges to improve supervision of the country's food and drug industries, but incidents have nevertheless erupted since then.

One of the biggest scandals emerged in 2008 when huge amounts of the industrial chemical melamine were found to have been illegally added to dairy products, killing at least six babies and sickening another 300,000.

More recently in September, the government arrested 32 people over the sale of cooking oil made from leftovers taken from gutters. (c) 2011 AFP

<http://medicalxpress.com/news/2011-11-china-hospital-disposes-baby.html>

China hospital disposes of live baby

Health authorities in south China said Friday they were investigating a hospital medical team for mistakenly diagnosing a stillbirth and disposing of a baby that was alive.

The probe is taking place at the Nanhai Red Cross Hospital in the Guangdong provincial city of Foshan where the incident occurred on October 26, the Nanhai district health bureau said in a statement faxed to AFP.

According to the statement, Liu Dongmei - eight months pregnant - had been rushed to the hospital with internal bleeding and stomach cramps. She later had an emergency birth, but the baby was neither breathing nor crying after leaving the womb and its skin had turned purple, it said. Believing it was dead, the medical team disposed of the child but did not follow proper hospital procedures, the statement added.

The Foshan News, a local website, reported that when Liu's sister-in-law asked to see the body around 30 minutes after birth, she was handed a yellow plastic bag containing the infant and found it was still alive.

"I opened the plastic bag and saw the baby's hands and feet moving, the stomach was going up and down and air bubbles were coming out of his mouth," the paper quoted her as saying. She was further shocked when she saw the baby was a boy - not a girl as the family had been told, it said. According to the Foshan News, nurses had told the family the child was a girl in an effort to blunt the blow of its death. In China, baby boys are often viewed as more precious than girls, as many families can have only one child as part of the nation's population policy and desire a male heir.

Following the discovery, the newborn was rushed to intensive care where he remains in a stable condition.

Officials at the hospital refused to comment on the incident when contacted by AFP.

China's healthcare system - once widely praised for improving the health of millions - is now panned as costly, underfunded and providing shoddy treatment, especially in poorer regions. Liu and her husband are seeking to sue the hospital for 300,000 yuan (\$45,000), the Beijing News said. The head of the maternity ward, a doctor and two nurses have been suspended pending the results of the investigation, it added. (c) 2011 AFP

<http://nyti.ms/sBONbm>

Three New Elements Named: Darmstadtium, Roentgenium and Copernicium

Calling Tom Lehrer.

By DENNIS OVERBYE

"There's antimony, arsenic, aluminum, selenium/And hydrogen and oxygen and nitrogen and rhenium..."

So starts the 1959 song "[*Elements*](#)," in which the Harvard math professor and musician set the periodic table to music. But now the old chestnut, beloved by science students for the last half century, needs more verses: Three newly discovered elements were given names on Friday by the General Assembly of the International Union of Pure and Applied Physics at a meeting in London.

They are Darmstadtium, or Ds, which has 110 protons in its nucleus and was named after the town in which it was discovered; Roentgenium, or Rg, with 111 protons, named after the discoverer of X-rays Wilhelm Conrad Roentgen; and Copernicium, or Cn, which has 112 protons and is named after the Polish astronomer Copernicus, who disrupted the view that the Earth was the center of the universe.

None of these elements occur in nature, or even last very long once created. They were all made in Darmstadt, Germany, at the Society for Heavy Ion Research Laboratory (Gesellschaft für Schwerionenforschung) by bombarding heavy nuclei with beams of other atoms.

**Researchers investigate link between autoimmune diseases and wounds that don't heal
Millions of Americans suffer from wounds that don't heal, and while most are typically associated
with diabetes, new research has identified another possible underlying cause - autoimmune
diseases.**

WASHINGTON, DC -- The finding represents an unappreciated link that could lead to important new insights in wound healing, say researchers at Georgetown University Medical Center.

The research will be presented during a poster session on Tuesday, Nov. 8, 2011, at the annual meeting of the American College of Rheumatology in Chicago.

The study was sparked by the keen observation of Georgetown rheumatologist Victoria Shanmugam, M.D., who began noticing something rather unusual in her patients with autoimmune diseases — any open wound they had was very slow to heal. Their recovery was even more protracted than in patients with wounds who have diabetes, a disease that is notoriously damaging to blood vessels and to normal skin repair.

So Shanmugam and her colleagues conducted a chart review of people who sought care at a high-volume wound clinic at Georgetown University Hospital to determine the prevalence of autoimmune diseases. The study included patients with open wounds — usually leg ulcers who were treated during a three-month period in 2009. Of the 340 patients, 49 percent had diabetes, which she says is a typical rate.

"But what was surprising is that 23 percent had underlying autoimmune diseases, and the connection between these relatively rare disorders and wounds that don't heal is under-recognized," she says.

Of the 78 patients in the cohort who had autoimmune disease, most had rheumatoid arthritis, lupus or livedoid vasculopathy, a type of vascular disease.

Shanmugam says her findings also show that autoimmune disease-associated wounds were significantly larger at the patient's first visit. These non-healing wounds can be "incredibly emotionally draining and financially costly," Shanmugam says, because they require doctor visits over many months as well as an ever-present risk of serious infections. Sometimes, infections can lead to surgery and the amputation of limbs. More often, they require skin grafts or use of skin substitutes, which may still not solve the problem.

In fact, Shanmugam's study found that skin grafts were more likely to fail in patients with autoimmune disease-associated wounds.

Shanmugam hopes the link she has made between autoimmune diseases and wound healing will make its way into the consciousness of the general practitioner. While it is much too invasive and costly to recommend that all patients with wounds be tested for autoimmune diseases, she says, "If a doctor has a patient with a leg ulcer that won't heal after three or four months and they have done all the appropriate treatments, I hope they will look for the presence of an autoimmune disorder."

Shanmugam's research is funded by a KL2 Mentored Career Development Program Scholar grant from Georgetown-Howard Universities Center for Clinical & Translational Science. The Center was established in 2010 and is funded by a National Institutes of Health Clinical and Translational Science Award. The KL2 grant funds junior faculty members starting translational research programs.

