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University of Maryland School of Medicine publishes scientific paper on 2001 anthrax attacks

Institute for Genome Sciences led pioneering investigation in new field of microbial forensics

Researchers at the Institute for Genome Sciences at the University of Maryland School of Medicine and collaborators at the FBI, the U.S. Army Medical Research Institute of Infectious Diseases and Northern Arizona University have published the first scientific paper based on their investigation into the anthrax attacks of 2001. The case was groundbreaking in its use of genomics and microbiology in a criminal investigation. More than 20 people contracted anthrax from Bacillus anthracis spores mailed through the U.S. Postal Service in 2001, and five people died as a result of the attacks. Research scientists from the Institute for Genome Sciences played a key role in the investigation known as Amerithrax. The work is a pioneering advance in the new field known as microbial forensics, a science that would likely play a key role in the investigations of any future bioterror attacks. The paper was published online today in the Proceedings of the National Academy of Sciences.

The paper describes how the Institute for Genome Sciences faculty and collaborators from the FBI found that the anthrax samples used in all the attacks were genetically identical. Later, another group of scientists - also including Institute for Genome Sciences faculty - would trace the anthrax spore used in the letters back to a flask of Bacillus anthracis and several samples taken from that flask. The primary custodian of the flask was Bruce Ivins, Ph.D., a scientist at a U.S. Army biodefense laboratory in Maryland. With this key investigative lead from the scientific team, the FBI used additional police work to conclude that Dr. Ivins was the perpetrator of the mail attacks. Dr. Ivins killed himself before the case could go to court. The FBI has since closed the Amerithrax investigation.

"This paper and the Amerithrax investigation really marked the beginning of a new approach for the science we call forensic genomics," says senior author Jacques Ravel, Ph.D., associate professor of microbiology and immunology at the University of Maryland School of Medicine and associate director for genomics at the Institute for Genome Sciences. "The science was a critical component of the Amerithrax case. Without genomics, it would have been extremely difficult to narrow the pool of potential suspects."

"Before Amerithrax, no one appreciated the precision, accuracy and reliability that this type of genomics can offer as a microbial forensic technique," says first author David Rasko, Ph.D., assistant professor for microbiology and immunology at the School of Medicine and a research scientist at the Institute for Genome Sciences. "To this day, this is still the only case in which microbiology and genomics have been used in a criminal investigation. Microbial forensics would be a critical investigative tool if another bioterror attack were ever to strike the U.S."

The newly published paper describes the work that the FBI assigned to Institute for Genome Sciences faculty members including Drs. Ravel and Rasko as well as the institute's director, Claire Fraser-Liggett, Ph.D., professor of medicine and microbiology and immunology at the School of Medicine, from 2001 through 2003. The scientists worked with a team of investigators including Paul Keim, Ph.D., regents professor and division director at Northern Arizona University and the Translational Genomics Research Institute, as well as military and FBI investigators.

"We have assembled a world-class team of genomics researchers at the Institute for Genome Sciences," says E. Albert Reece, M.D., Ph.D., M.B.A, vice president for medical affairs, University of Maryland, and John Z. and Akiko K. Bowers Distinguished Professor and dean, University of Maryland School of Medicine. "Their pioneering work in the field of microbial forensics is typical of their cutting-edge research. We are proud to have them on our team, leading us into a new age of science."

The scientific investigation began by asking if the anthrax used in all the letters had come from the same source. The spores in each letter had been prepared differently, making them look different from one another to the naked eye. Military scientists at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) at Fort Detrick, Md., took spores from each letter and grew them in the laboratory. Looking with an expert eye at the samples they had grown, the scientists could see that a small number of the bacterial colonies looked very different from the ordinary appearance of most of the anthrax bacteria. The scientists isolated those unusual spores and grew them alone. As the spores replicated, the scientists saw that the differences or variations persisted, indicating that they were not some kind of aberration.

"Samples from the letters had the same combination of variants in the spores," said Dr. Ravel. "That was one of the first things that began to link the letters."

Next, Institute for Genome Sciences researchers were charged with sequencing the genome of those populations of variant bacterial colonies - just those spores that looked unusual. They wanted to find out if there were genetic differences that were making the colonies of bacteria look unique. There were, and those same

genetic differences were found the spore preparations from all the letters, conclusively linking them to the same source. There were four types of these variations found in the anthrax that came in the letters. Scientists eventually discovered that the anthrax used in the attacks was the product of at least two different production batches of anthrax that had been mixed together, each with its own unique distribution of variants. Mixing the batches created a unique combination of genetic signatures that later helped them track the spore preparations back to the source flask in the lab of Dr. Ivins.

"This data we uncovered acted like a genetic fingerprint," says Dr. Keim, of Northern Arizona University. "It could link microbial evidence to its potential source. The science was one technique used to generate leads as part of a larger FBI investigation," says Dr. Ravel. "Science tells us the spore came from that particular flask, but it's important to note that the science never pointed to Bruce Ivins. It was police work that did that."

As one of the first and most high-profile investigations of its kind, Amerithrax has helped to shape the emerging field of microbial forensics. Since the case, Dr. Ravel, Dr. Rasko and their colleagues at the Institute for Genome Sciences have been leaders in the scientific community's effort to expand the field by contributing to the development of standards and guidelines for future investigations.

"We were figuring this out as we went along," says Dr. Rasko. "For example, to produce evidence that will hold up in criminal court, you need a very high standard of accuracy with well validated methodologies. It is a much higher standard than our own academic research. Your results need to be completely foolproof and stand in a court of law. Those are the kinds of standards and guidelines we're developing now, so that microbial forensic scientists can be prepared in the event of another biological attack."

http://www.eurekalert.org/pub_releases/2011-03/drnl-bsa030711.php

BESC scores a first with isobutanol directly from cellulose

OAK RIDGE, Tenn. - ***In the quest for inexpensive biofuels, cellulose proved no match for a bioprocessing strategy and genetically engineered microbe developed by researchers at the Department of Energy's BioEnergy Science Center.***

Using consolidated bioprocessing, a team led by James Liao of the University of California at Los Angeles for the first time produced isobutanol directly from cellulose. The team's work, published online in Applied and Environmental Microbiology, represents across-the-board savings in processing costs and time, plus isobutanol is a higher grade of alcohol than ethanol.

"Unlike ethanol, isobutanol can be blended at any ratio with gasoline and should eliminate the need for dedicated infrastructure in tanks or vehicles," said Liao, chancellor's professor and vice chair of Chemical and Biomolecular Engineering at the UCLA Henry Samueli School of Engineering and Applied Science. "Plus, it may be possible to use isobutanol directly in current engines without modification."

Compared to ethanol, higher alcohols such as isobutanol are better candidates for gasoline replacement because they have an energy density, octane value and Reid vapor pressure - a measurement of volatility - that is much closer to gasoline, Liao said.

While cellulosic biomass like corn stover and switchgrass is abundant and cheap, it is much more difficult to utilize than corn and sugar cane. This is due in large part because of recalcitrance, or a plant's natural defenses to being chemically dismantled. Adding to the complexity is the fact biofuel production that involves several steps - pretreatment, enzyme treatment and fermentation - is more costly than a method that combines biomass utilization and the fermentation of sugars to biofuel into a single process.

To make the conversion possible, Liao and postdoctoral researcher Wendy Higashide of UCLA and Yongchao Li and Yunfeng Yang of Oak Ridge National Laboratory had to develop a strain of Clostridium celluloyticum, a native cellulose-degrading microbe, that could synthesize isobutanol directly from cellulose. "This work is based on our earlier work at UCLA in building a synthetic pathway for isobutanol production," Liao said.

While some Clostridium species produce butanol, these organisms typically do not digest cellulose directly. Other Clostridium species digest cellulose but do not produce butanol. None produce isobutanol, an isomer of butanol. “In nature, no microorganisms have been identified that possess all of the characteristics necessary for the ideal consolidated bioprocessing strain, so we knew we had to genetically engineer a strain for this purpose," Li said.

While there were many possible microbial candidates, the research team ultimately chose Clostridium cellulolyticum, which was originally isolated from decayed grass. The researchers noted that their strategy exploits the host's natural cellulolytic activity and the amino acid biosynthetic pathway and diverts its intermediates to produce higher alcohol than ethanol.

The researchers also noted that Clostridium cellulolyticum has been genetically engineered to improve ethanol production, and this has led to additional more detailed research. Clostridium cellulolyticum has a

sequenced genome available via DOE's Joint Genome Institute. This proof of concept research sets the stage for studies that will likely involve genetic manipulation of other consolidated bioprocessing microorganisms.
The paper is titled "Metabolic Engineering of Clostridium Cellulolyticum for Isobutanol Production from Cellulose," and is available online at http://aem.asm.org/.

http://www.eurekalert.org/pub_releases/2011-03/wfub-lui030311.php

Laboratory-grown urethras implanted in patients, scientists report

WINSTON-SALEM, NC - *Researchers at the Institute for Regenerative Medicine at Wake Forest University Baptist Medical Center and colleagues reported today on a new advance in tissue engineering.*

The team is the first in the world to use patients' own cells to build tailor-made urinary tubes and successfully replace damaged tissue. In an article published Online First by The Lancet, the research team reports replacing damaged segments of urinary tubes (urethras) in five boys. Tests to measure urine flow and tube diameter showed that the engineered tissue remained functional throughout the six-year (median) follow-up period.

"These findings suggest that engineered urethras can be used successfully in patients and may be an alternative to the current treatment, which has a high failure rate," said Anthony Atala, M.D., senior author, director of the Wake Forest Institute for Regenerative Medicine and a pediatric urologic surgeon. "This is an example of how the strategies of tissue engineering can be applied to multiple tissues and organs."

Atala's team used a similar approach to engineer replacement bladders that were implanted in nine children beginning in 1998, becoming the first in the world to implant laboratory-grown organs in humans. Researchers at the institute are currently working to engineer more than 30 different replacement tissues and organs.

Defective urethras can be the result of injury, disease or birth defects. While short defects in the tube are often easily repairable, larger defects can require a tissue graft, usually taken from skin or from the lining of the cheek. "These grafts, which can have failure rates of more than 50 percent, often become narrowed, leading to infections, difficulty urinating, pain and bleeding," said Atlantida-Raya Rivera, lead author and director of the HIMFG Tissue Engineering Laboratory at the Metropolitan Autonomous University in Mexico City.

Between March 2004 and July 2007, the research team built engineered urethras for five boys, ages 10 to 14, using the patients' own cells. Three patients had widespread injury due to pelvic trauma and two patients had previous urethra repairs that had failed. The engineered tubes were used to replace entire segments of damaged urethra in the section that runs between the penis and the prostate (posterior section) -- considered the most difficult to repair.

The first step in engineering the replacement urethral segments was taking a small (one-half inch by one-half inch) bladder biopsy from each patient. From each sample, scientists isolated smooth muscle cells and endothelial cells, the cells that line blood vessels and other tubular structures. These cells were multiplied in the lab for three to six weeks and were then placed on a three-dimensional scaffold shaped like a urethral tube. Smooth muscle cells were placed on the outside of the scaffold and endothelial cells on the inside. The scaffolds, which were sized for each individual patient, were made of a biodegradable mesh material. After cell placement, the scaffolds were incubated for seven days - with the total time for construction ranging from four to seven weeks. By day six, all surface areas were completely covered with cells.

After incubation, the tubes were surgically implanted by removing the defective segment of the urethra and scar tissue and sewing the replacement tubes in place. Once in the body, the cells continued to expand and tissue formation began. Biopsies showed that the engineered urethras had normal layers of epithelial and smooth muscle within three months after implantation. Flow measurements, urine tests and patient questionnaires confirmed patient satisfaction as measured by lack of nighttime leaking, straining to urinate, and urinary tract infections - common symptoms when urethral tubes become narrowed.
The research was supported in part by the National Institute of Diabetes and Digestive and Kidney Diseases. Co-researchers were James J. Yoo and Shay Soker, with Wake Forest Baptist, and Diego R. Esquiliano and Esther Bayghen, with Metropolitan Autonomous University, Mexico.

http://www.eurekalert.org/pub_releases/2011-03/osu-wud030711.php

Web use doesn't encourage belief in political rumors, but e-mail does

COLUMBUS, Ohio - *Despite the fears of some, a new study suggests that use of the internet in general does not make people more likely to believe political rumors.*

However, one form of internet communication - e-mail - does seem to have troubling consequences for the spread and belief of rumors.

"I think a lot of people will be surprised to learn that using the internet doesn't necessarily promote belief in rumors. Many people seem to think that's self-evident," said R. Kelly Garrett, author of the study and assistant professor of communication at Ohio State University.

"The internet does make it easier to circulate rumors, but going online doesn't make us more gullible."

However, e-mail is a special case. People are much more likely to believe false rumors that they receive in e-mails from friends and family. People seem to be wary about rumors they read on websites and blogs, Garrett said. They are more likely to check these rumors to see if they are correct.

"The problem is that we are more likely to let our defenses down when we're dealing with our friends, which is why e-mail can have such harmful consequences. We don't normally question what our friends tell us," he said.

His findings will appear in the April 2011 issue of the journal Human Communication Research.

The study involved a telephone survey of 600 Americans in November 2008, immediately after the presidential election. Participants were asked about their exposure to 10 rumors that were circulating about the two major presidential tickets, Obama-Biden and McCain-Palin.

The rumors included eight patently false statements, ones that were rejected by both presidential candidates and by major fact-checking organizations such as FactCheck.org. Participants were also asked about two true statements. Some of the false rumors included "Barack Obama is a Muslim" and "While serving as the Mayor of Wasilla, Alaska, Sarah Palin successfully banned several books from the local library."

Results showed that use of the internet and online sources of political information did indeed lead people to encounter more rumors about the candidates. And the more rumors someone heard, the more they believed. In fact, for every two additional rumors that a person heard, the average number of rumors believed increased by about one.

However, people were also more likely to see rebuttals to the rumors online, as well, Garrett said. In the end, the overall internet use had very little effect on the number of rumors someone believed.

However, it was when Garrett separated the various online sources of political news that he found each source had different types of influence. For example, results showed that the use of voter information websites and the websites of major news organizations was not linked to rumor exposure. However, use of political blogs and e-mail from friends and family was linked to seeing more rumors.

The use of e-mail led to a particularly vicious feedback loop of rumor-mongering, Garrett said. The more political e-mails that participants received from friends and family during the 2008 election, the more rumors they were likely to believe. And the more rumors they believed, the more political e-mails they sent.

In addition, receiving e-mails only promoted belief in rumors about the candidate whom the person opposed, the study found. And people were more likely to share e-mails as belief in rumors about the opposed candidate increased. "It is a self-reinforcing process that seems to amplify rumor beliefs through repetition," Garrett said. "We have people who are biased to accept the rumors they receive from friends, which leads them to forward the e-mail to other friends, who repeat the process over and over again." All of this contributes to the survival of rumors, despite the overwhelming evidence against them, and helps fuel the partisan divide in the country, he said.

Garrett noted that this study didn't include specific investigation of Facebook and Twitter, which have exploded in popularity in recent years. But he said both of these are social networks that allow us to communicate directly with friends, much like we do with e-mail. "It seems reasonable to expect that the same characteristics that make e-mail so conducive to spreading rumors apply to both Facebook and Twitter, as well," he said.

Garrett said he believes that, overall, the results offer a mixed bag for those who worry about the effect of the internet on the spread of rumors. "It could have been worse," he said. "While the effect of e-mail is troubling, there are plenty of people who encounter rumors on the web every day and dismiss them."

The research was supported by the National Science Foundation.

http://www.eurekalert.org/pub_releases/2011-03/foas-rsd030711.php

Rockefeller Scientists discover new compound that rids cells of Alzheimer protein debris

New research in the FASEB Journal suggests that a compound called SMER28 reduces beta-amyloid by stimulating autophagy, which effectively slows the buildup of toxic beta-amyloid

If you can't stop the beta-amyloid protein plaques from forming in Alzheimer's disease patients, then maybe you can help the body rid itself of them instead. At least that's what scientists from New York were hoping for when they found a drug candidate to do just that. Their work appears in a research report online in The FASEB Journal (http://www.fasebj.org), and shows that a new compound, called "SMER28" stimulated autophagy in rat and mice cells. Autophagy is a process cells use to "clean out" the debris from their interior, including unwanted materials such as the protein aggregates that are hallmarks of Alzheimer's disease. In mice and rat cells, SMER28 effectively slowed down the accumulation of beta-amyloid.

"Our work demonstrates that small molecules can be developed as therapies, by activating a cellular function called autophagy, to prevent Alzheimer's disease," said Paul Greengard, Ph.D.,Nobel laureate and director of the Laboratory of Molecular and Cellular Neuroscience at The Rockefeller University in New York, NY. "By

increasing our understanding of autophagy, it might be possible to stimulate it pharmacologically or naturally to improve the quality of life for aging people."

Using mouse and rat cells, scientists tested various compounds for their ability to reduce the buildup of beta-amyloid by exposing cultured cells to compounds known to activate autophagy. The effects of these compounds were then compared by removing growth factors from the culture medium. Researchers then focused on the most effective compound, which was SMER28, to characterize the cellular components involved in this phenomenon. For that purpose, the effect of SMER28 on beta-amyloid formation was compared using normal cells or cells where the expression of genes known to be involved in autophagy was reduced or abolished. Results showed involvement of three important autophagic players, and one was essential for the effect of SMER28. This research represents a radically different approach to treating Alzheimer's disease, namely boosting a cellular mechanism to enhance the clearance of beta-amyloid, as well as other protein aggregates; and it opens a new therapeutic avenue for the treatment of this and other degenerative diseases.

"Autophagy has been called the cell's equivalent of urban renewal. In that sense, SMER28 functions as a cellular forklift to clear out unwanted debris," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "The Rockefeller group shows that strategies to remove the blight in cells that causes Alzheimer's disease are not only worth pursuing, but so far, appear to be very promising."

http://www.newscientist.com/article/dn20216-nasa-should-bring-mars-rocks-back-to-earth-says-panel.html

NASA should bring Mars rocks back to Earth, says panel

*** 01:26 08 March 2011 by David Shiga**

Bringing Mars rocks to Earth should be a top priority for NASA in the coming decade, says a high-level panel of planetary scientists.

It also recommended a mission to Jupiter's icy moon, Europa, thought to harbour an ocean of liquid water beneath its surface. But if the agency cannot afford such multi-billion-dollar "flagship" missions, they should be delayed in favour of smaller missions, the panel says. The panel's recommendations are not binding, but the report is likely to strongly influence NASA's decisions.

As its name implies, the Planetary Science Decadal Survey is organised just once every 10 years by the National Academy of Sciences. It ranks the importance of missions to study planets and other objects in the solar system, excluding the sun and Earth. The report, released on Monday, covers the decade from 2013 to 2022.

Searching for life

It recommends that NASA make a Mars sample return mission its top priority among its large planetary science missions. Bringing Martian rocks back to Earth would allow scientists to study them with a much wider array of instruments than can be packaged on a Martian rover. That in turn would allow scientists to better search for signs of past or present life, the report says.

"If we are to advance our fundamental knowledge of whether life has existed elsewhere in the solar system, we have to bring samples back," agrees Jack Mustard of Brown University in Providence, Rhode Island, who was not a member of the panel. "We could go on for another 50 years sending rovers, but I think the next ultimate step in our understanding will come from sample return."

Because of budget limitations, the panel recommended moving forward only with the first stage of such a sample return mission in the coming decade - a rover called Mars Astrobiology Explorer-Cacher (MAX-C) that would find and collect the samples. A second mission could later be sent to launch these samples into Mars orbit, while a third mission would bring them back to Earth. MAX-C is estimated to cost $3.5 billion but the panel hopes NASA can tweak its design to shave $1 billion off that price tag.

Subsurface ocean

The panel's second-highest priority for large missions is a probe that would orbit Europa. It would assess the moon's potential for hosting life by trying to confirm the presence of an ocean and determining how far the ocean lies below the moon's icy surface. The mission, estimated to cost $4.7 billion, would also study the surface to help identify interesting landing sites for future missions. NASA has already been studying the concept as part of a possible joint mission with the European Space Agency, which would supply an orbiter for Ganymede, another icy moon of Jupiter with a possible ocean beneath its surface.

Other large missions that the panel recommended, though at a lower priority than the Mars sample return and Europa missions, include:

- An orbiter and atmospheric probe for Uranus
- An orbiter for Saturn's icy moon, Enceladus, which may have a reservoir of liquid water beneath its surface
- An orbiter to study Venus's climate

The panel also encouraged moving forward with a small mission called the Mars Trace Gas Orbiter, which would try to determine the source of methane observed on Mars, which some scientists say could be due to life, though it could also be produced by water-rock interactions that do not involve life. NASA and the European Space Agency are already planning to launch such a mission in 2016. The report made a short list of the most important medium-size missions to fly at the next opportunity, including:

· A comet surface sample return

· A sample return from the giant impact scar at the moon's south pole, which could test the idea that a barrage of impactors struck the inner solar system 3.9 billion years ago

· An atmospheric probe for Saturn

· A mission to the so-called Trojan asteroids that share Jupiter's orbit

· Venus explorer that would drop into the planet's atmosphere

How many of the large, medium, and small missions actually fly depends on NASA's uncertain future budgets. If money turns out to be really tight, the panel recommended postponing some or all of the large missions rather than eliminating the small- and medium-sized missions.

http://www.eurekalert.org/pub_releases/2011-03/jgh-cid030311.php

Conflicts-of-interest in drug studies sneaking back into medical journals, say investigators

'Studies of studies' can hide financial conflicts-of-interest with drug makers

Hidden financial conflicts-of-interest are sneaking into published drug research through the back door, warns an international team of investigators, led by researchers from the Jewish General Hospital's Lady Davis Institute for Medical Research and McGill University in Montreal. More and more, policy decisions and what medications doctors prescribe for their patients are being driven by large "studies of studies," called meta-analyses, which statistically combine results from many individual drug trials.

Led by Dr. Brett Thombs and McGill graduate student Michelle Roseman, the team found that important declarations of financial conflicts-of-interest in individual drug trials disappeared when those studies were combined in meta-analyses. Their results will be published in the March 9 issue of the Journal of the American Medical Association (JAMA).

Roseman, the study's first author, and the rest of the team reviewed 29 recent meta-analyses on a range of drug treatments published in high-impact medical journals. Those 29 meta-analyses, or "studies of studies," included results from 509 drug trials. The team documented the funding sources and author-industry financial ties of all 509 trials and whether or not the meta-analyses noted who had funded the trials.

"Only 2 of the 29 meta-analyses even mentioned the issue of who funded the original drug trials, and even those 2 did it in very obscure places in the published articles," said Thombs, a psychologist and assistant professor in the Department of Psychiatry at McGill University. "Not one of the meta-analyses mentioned whether researchers who conducted the trials were employed by industry or personally received money from industry."

"Most people want their physicians to make treatment decisions based on high-quality, unbiased evidence," said Roseman. "Researchers who conduct meta-analyses should be aware of who funds the trials they review and they should assess the risk that findings might be biased due to drug company sponsorship."

The team identified 7 meta-analyses where every single drug trial included was paid for, at least in part, by the maker of the drug or had investigators linked financially to drug makers. In 6 of the 7 meta-analyses, however, there was no mention of who funded the drug trials.

"Consumers can be more confident that drugs actually work if there is at least 1 independent evaluation that confirms this," said Thombs. "When all existing studies are financially linked to drug makers, there is a risk that patients and their physicians may be misled."

"What is surprising is that many researchers who do meta-analyses don't seem to be aware of these important issues," added Roseman. "We surveyed the authors of the 29 meta-analyses. Only 7 said that they even recorded who funded the drug trials they evaluated, and only 2 published this information. Furthermore, only 2 recorded author-industry financial ties, and none published this."

Thombs, Roseman and their colleagues have called for changes in policy on how evidence on drug treatments is reported in meta-analyses. "Unless we require authors of meta-analyses to provide this information for consumers, it will be lost," emphasized Thombs. "Patients and doctors want to have this information, and we believe it is in the best interest of all of us to make sure it is available."

"Few people would buy a car whose performance and safety had only been tested by the manufacturer or a house based only on the word of the seller without an independent inspection," added Thombs. "Yet most drugs

that people take have been evaluated, for the most part, by the companies that produce them and profit from their sales. At the very least, doctors and their patients need to know who is evaluating the effectiveness and safety of drugs that are being prescribed."

The Canadian Institutes of Health Research and the Fonds de la Recherche en Santé Québec provided funding that supported work on this study. In addition to Thombs and Roseman, other researchers who contributed to this study were Katherine Milette, a McGill graduate student; Lisa A. Bero, Ph.D., of the University of California, San Francisco; James C. Coyne, Ph.D. of the University of Pennsylvania, Philadelphia and the University of Groningen, the Netherlands; Joel Lexchin, M.D. of York University, University of Toronto, and University Health Network, Toronto; and Erick H. Turner, M.D., of the Oregon Health and Science University, Portland.

http://www.eurekalert.org/pub_releases/2011-03/uocd-rfd030811.php

Researchers find drug that stops progression of Parkinson's disease in mice

Medication turns on critical gene, protects brain cells

AURORA, Colo. - In a major breakthrough in the battle against Parkinson's disease, researchers at the University of Colorado School of Medicine have discovered a drug that stops the progression of the degenerative illness in mice and is now being tested in humans.

"Drugs currently used to treat Parkinson's disease just treat symptoms; they do not stop the disease from getting worse," said senior author Curt Freed, MD, who heads the division of Clinical Pharmacology and Toxicology at the CU School of Medicine. "We've now discovered that we can prevent the progression of the disease by turning on a protective gene in the brain."

Lead author Wenbo Zhou, PhD, Assistant Professor of Medicine, and Freed, a national pioneer in Parkinson's research, have found that the drug phenylbutyrate turns on a gene that can protect dopamine neurons in Parkinson's disease. The gene, called DJ-1, can increase production of antioxidants like glutathione to reduce the debilitating effects of excess oxygen in brain cells. In addition, activating DJ-1 helps cells eliminate abnormal proteins that otherwise accumulate and kill brain cells. Dopamine neurons are particularly susceptible to too much oxygen and abnormal protein deposits. Parkinson's disease is caused by dying midbrain dopamine neurons.

Zhou and Freed have studied the DJ-1 gene since 2003 when a European group discovered that mutations in DJ-1 could cause Parkinson's disease. The Colorado scientists immediately started work to see why the gene was so important and have published a series of papers on the subject since 2005. But to convert their findings into a practical treatment for Parkinson's disease, they needed to find a drug to turn on the DJ-1 gene.

"We know some drugs can turn on genes. For example, steroids like testosterone act on genes in muscle cells to create muscle bulk," said Freed. After testing many drugs, the team found that phenylbutyrate could activate DJ-1 and keep dopamine neurons from dying. Next, they put the drug in the drinking water of mice genetically programmed to get Parkinson's disease as they aged.

Aging mice receiving the drug were able to move normally, had no decline in mental function, and their brains did not accumulate the protein that causes Parkinson's. By contrast, older animals that did not get the drug saw a steady decline in their ability to move as their brains were damaged by abnormal proteins. The researchers began giving phenylbutyrate to people in 2009, to test the safety of the drug in Parkinson patients.

Zhou and Freed will publish the human results in the coming months.

"We look forward to a future when Parkinson patients will be able to take a pill that will turn on the DJ-1 gene and stop the progressive disability associated with the illness," Freed said. "Right now, when you get the diagnosis of Parkinson's, you can expect to have a steady decline in the ability to move. While drugs like L-DOPA are very important for generating dopamine in the brain and making movement possible, these drugs have little impact on the ongoing deterioration of the patients' own brain cells."

Over one million people in the United State have the disease which usually strikes those in their 50s and 60s. Patients have a decline in their ability to walk, talk, and write because of slow movement and rigid muscles. They develop tremors and reflexes slow down. The current treatment of Parkinson's is based on drugs that increase dopamine production in the brain.

Freed is a national leader in transplanting dopamine cells into the human brain to relieve symptoms. He and his neurosurgical colleague Robert Breeze, MD, have done the operation in 61 patients, more than any other group in the world. The procedure can replace the need for drugs but even cell transplants do not prevent the progression of the disease.

Freed and Zhou are now looking for other drugs that might turn on the DJ-1 gene. One drawback of phenylbutyrate is that patients must take very large doses, 16 grams per day or 32 large tablets taken at frequent intervals. While the drug is approved by the FDA for treating a rare genetic disease in infants, whether it can stop Parkinson's in people remains to be seen.

But Zhou and Freed believe the discovery offers new hope for those suffering from Parkinson's disease.

"If we can say to someone that as of today we can stop your disease from getting worse, that would be a truly significant achievement," Freed said. The results have been published on line in the Journal of Biological Chemistry, ***http://www.jbc.org/content/early/2011/03/03/jbc.M110.211029.full.pdf+html***.

http://www.eurekalert.org/pub_releases/2011-03/uonc-usf030811.php

UNC study finds oral tongue cancer increasing in young, white females

Chapel Hill, NC - *A UNC study released this week in the Journal of Clinical Oncology finds an increasing incidence of squamous cell carcinoma of the oral tongue in young white females in the United States over the last three decades.*

A team of researchers from UNC Lineberger Comprehensive Cancer Center analyzed data from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) database and found that, between 1975 and 2007, the overall incidence for all ages, genders, and races of the disease was decreasing. However, the incidence of oral tongue squamous cell carcinoma rose 28 percent among individuals ages 18 to 44. Specifically, among white individuals ages 18 to 44 the incidence increased 67 percent. The increasing incidence was most dramatic for white females ages 18 to 44. They had a percentage change of 111 percent. Interestingly, the incidence decreased for African American and other racial groups.

Historically, oral tongue cancer has been strongly associated with heavy tobacco and alcohol use. Other epidemiological studies have related the decreasing incidence of oral tongue cancer in the United States to the decreased use of tobacco products. Though the UNC research team verified the known decreasing incidence of oral tongue cancer, they were surprised to observe an increasing incidence in young white individuals, specifically young white females.

"Lately we have been seeing more oral tongue cancer in young white women in our clinic. So we looked at the literature, which reported an increase in oral tongue squamous cell carcinoma in young white individuals but couldn't find any information about gender-specific incidence rates, so we decided we should take a look at the SEER data," said Bhisham Chera, MD, lead author on the study and assistant professor in the Department of Radiation Oncology.

Over the past decade an association between the human papilloma virus with squamous cell carcinoma of the tonsil and tongue has been observed. Patients with human papilloma virus associated oral squamous cell carcinoma are typically male, white, non-smokers, non-drinkers, younger in age and have higher socioeconomic status. The researchers at UNC have preliminarily tested the cancers of the oral tongue of their young white female patients and have not found them to be associated with the virus. Other institutions have also noted the absence of the virus in young females with oral tongue cancer. The UNC researchers have also anecdotally observed that these young white female patients are typically non-smokers and non-drinkers.

"Our findings suggest that the epidemiology of this cancer in young white females may be unique and that the causative factors may be things other than tobacco and alcohol abuse. Based on our observations and the published data, it appears that these cases may not be associated with the human papilloma virus. We are actively researching other causes of this cancer in this patient population." he added.

Though the increasing rate of oral tongue cancer in young white females is alarming oral tongue cancer is a rare cancer, relative to breast, lung, prostate, and colorectal cancer. "Primary care physicians and dentist should be aware of this increasing incidence and screen patients appropriately," states Dr. Chera. Oral tongue cancer is typically treated with surgery first followed by radiation and, in some cases, chemotherapy.

Other UNC Lineberger researchers who contributed to the study include Sagar Patel, BA, of the Department of Radiation Oncology, William R. Carpenter, PhD, MHA, professor of health policy and management in the UNC Gillings School of Global Public Health, Marion Couch, MD, PhD, formerly a professor of otolaryngology/head & neck surgery at UNC (now at the University of Vermont), Mark Weissler, MD, distinguished professor of otolaryngology/head & neck surgery, Trevor Hackman, MD, assistant professor of otolaryngology/head & neck surgery, D. Neil Hayes, MD, MPH, associate professor in the division of hematology/oncology, and Carol Shores, MD, PhD, associate professor of otolaryngology/head & neck surgery.

http://www.eurekalert.org/pub_releases/2011-03/uol-rcp030811.php

Roundworm could provide new treatment for sepsis

Research by the University of Liverpool has found that systemic inflammation caused by sepsis can be suppressed by a protein which occurs naturally in a type of roundworm.

Sepsis is a serious inflammatory condition, caused by the body over-reacting to infection. The body becomes overwhelmed by bacteria, setting off a series of reactions that lead to inflammation and clotting. It affects around 20 million people worldwide each year, and accounts for a large proportion of intensive care unit admissions.

For the past 30 years, sepsis has largely been treated by antibiotics and maintenance of blood flow. Despite these treatments - often complicated by antibiotic-induced liver injury or the presence of multi drug-resistant bacteria - mortality rates for those with severe illness who go into multi-organ damage and septic shock, remain as high as 50%. New treatments for septic shock are of high clinical need.

Findings by an international team, led by Professor Alirio Melendez, based at the University's Medical Research Council Centre for Drug Safety Science in the Institute of Translational Medicine, show that inflammation triggered by bacterial endotoxins in immune cells from patients with sepsis is suppressed by a protein called ES-62 which is secreted by a type of roundworm called Acanthocheilonema viteae.

Roundworms can infect the human digestive tract, lymphatic vessels, skin and muscle. They are extremely common - particularly in parts of the world with poor sanitation - and it is estimated that nearly a quarter of the world's population are currently infected. Roundworm can live in the human body for decades without adverse effects or triggering the immune system.

Scientists already know that the protein secreted by roundworm is capable of suppressing inflammation and people infected with worms usually benefit from reduced inflammation if they suffer from conditions such as allergies and autoimmune diseases.

Professor Melendez explained: "The protein secreted by the roundworm stimulates a process called autophagy, a process of 'self-eating' that is essential to clear damage to cellular proteins or organelles and promote cell survival and function during stress situations. "Autophagy reduces inflammation but at the same time permits the clearance of microbial infection. The findings suggest that ES-62 could be used to induce autophagy and reduce the overwhelming inflammation that is responsible for the massive tissue damage seen in sepsis."

He added: "ES-62 has the therapeutic ability to enhance recovery in septic shock by suppressing and limiting catastrophic inflammatory responses while allowing for bacterial clearance to occur. Administration of ES-62, or a synthetic small molecule derivative, alone or in combination with antibiotics could potentially be used treatment of septic shock as well as other inflammatory diseases."

The research is published in Nature Immunology and was carried out in collaboration with colleagues from the Universities of Strathclyde, Glasgow and the National University of Singapore.

http://www.eurekalert.org/pub_releases/2011-03/osu-pnr030811.php

Passive news reports may lead readers to feel they can't find the truth

COLUMBUS, Ohio - *Passive news reporting that doesn't attempt to resolve factual disputes in politics may have detrimental effects on readers, new research suggests.*

The study found that people are more likely to doubt their own ability to determine the truth in politics after reading an article that simply lists competing claims without offering any idea of which side is right.

"There are consequences to journalism that just reports what each side says with no fact checking," said Raymond Pingree, author of the study and assistant professor of communication at Ohio State University.

"It makes readers feel like they can't figure out what the truth is. And I would speculate that this attitude may lead people to tune out politics entirely, or to be more accepting of dishonesty by politicians."

The study appears in the current issue of the Journal of Communication.

While some disputes in politics involve subjective issues where there is no right or wrong answers, some involve factual issues that could be checked by reporters if they had the time and the desire, Pingree said.

"Choosing among government policies is simply not like choosing among flavors of ice cream. Policy questions quite frequently center on facts, and political disputes can and often do hinge on these facts, not only on subjective matters," he said. For example, when opponents of Obama's health care bill claimed it contained provisions for "death panels" that would determine who is worthy of health care, reporters could check the text of the bill to see if such a provision existed, Pingree said.

Pingree noted that many critics have condemned the media for playing too passive a role in factual disputes, but this is the first study to look at how such reporting actually affects readers, at least in terms of politics.

To find out how passive reporting affects audiences, Pingree conducted an experiment with 538 college students. All of the students were asked to read one of four versions of a fictional news story about a fictional health care bill under debate in the House of Representatives.

The stories were nearly identical and set up two factual debates about the bill. In one dispute, opponents of the bill claimed that its cost will be far higher than the estimated $200 million and in the other, opponents claimed that the bill is redundant with Medicaid and will create unnecessary bureaucracy. Two versions of the article simply mentioned the dispute, while the other two provided facts that showed which side was correct.

After they read the article, the participants answered a variety of questions, including three that probed whether they felt they could, in general, find the truth in matters of politics. For example, one question asked

how much the participants agreed with the statement "If I wanted to, I could figure out the facts behind most political disputes."

Results showed that people interested in the health care issue who read the passive article felt they were less able to find truth in politics, compared to those who read the article resolving who was right in the debate. "We're just beginning to explore this issue," Pingree noted. "But it is noteworthy that just reading a single news story about a single topic can affect how people feel about their own ability to find truth in politics." The issue of "he said/she said" journalism is especially critical today because many media outlets are understaffed and news cycles are faster than ever, meaning that reporters often have less time to check facts, he said.

Pingree emphasized that he is not being critical of all journalists. Many still do a good job of resolving factual disputes when they can. "But I think it is clear that this happens less than it used to. As a result, there may be people out there who feel like there is no such thing as a political fact, or at least that they can't figure out what it is," he said. "That may make it easier for people to just quit following politics at all, or to accept dishonesty in politicians."

Pingree said the results suggest that readers want reporters to tell them when the facts support - or don't support -- one side or the other. He noted that there are now journalistic websites such as PolitiFact.com that are dedicated just to resolving factual disputes in politics.

"It is interesting that there are now institutions within journalism dedicated to resolving disputes. A few decades ago, that was seen as the role of all journalists. Journalists didn't see themselves as stenographers, but as judges, keeping the lawyers honest in the court of public opinion. We don't see that as much anymore."

http://www.bbc.co.uk/news/uk-12663183

Food sold in recycled cardboard packaging 'poses risk'

By Nick Higham BBC News

Leading food manufacturers are changing their packaging because of health concerns about boxes made from recycled cardboard, the BBC has learned.

Researchers found toxic chemicals from recycled newspapers had contaminated food sold in many cardboard cartons. The chemicals, known as mineral oils, come from printing inks. Cereal firm Jordans has stopped using recycled cardboard and other firms are to ensure their recycled packaging does not contain any toxic oils.

Kellogg's and Weetabix said they were taking steps to reduce the amount of mineral oil in their packaging.

Exposure to mineral oils has been linked to inflammation of internal organs and cancer.

Government scientists in Switzerland found quantities of mineral oils between 10 and 100 times above the agreed limit in foods like pasta, rice and cereals sold in cartons made from recycled cardboard.

'Frightening' potential

In one scientific paper they describe the potential for mineral oils to migrate into foodstuffs as "frightening".

However, the Swiss food safety authorities have concluded that consumers who eat a balanced and varied diet have no need to worry. In a statement Jordans said that, as an environmentally responsible company which had previously used largely recycled packaging, it had taken the decision to abandon it reluctantly, but felt it was sensible.

The BBC investigation found other food companies were aware of the issue - but none had so far followed Jordans' lead.

More than half the cardboard used in Europe is made from recycled materials. So-called "virgin board" from newly harvested trees is more expensive and there is not enough of it to replace recycled card completely.

The research has been led by Dr Koni Grob at the government-run food safety laboratory of the Canton of Zurich. In one study for the German food ministry last year he and his colleagues tested a sample of 119 products bought from German supermarkets. They found mineral oils passed easily through many of the inner bags used to keep food dry and fresh. The longer a product stood on the shelves, the more mineral oil it was likely to absorb.

Dr Grob told the BBC: "Roughly 30 products from these 119 were free of mineral oil. "For the others they all exceeded the limit, and most exceeded it more than 10 times, and we calculated that in the long run they would probably exceed the limit 50 times on average and many will exceed it several hundred times."

The agreed safe limit for mineral oil saturated hydrocarbons, derived from an expert evaluation carried out for the UN's Food and Agriculture Organization and the World Health Organisation, is a migration of 0.6mg per kilogram.

Two effects

Studies on rats have highlighted the dangers to health of mineral oils.

Dr Grob said: "Toxicologists talk about two effects. One is the chronic inflammation of various internal organs and the other one is cancer." But he stressed consumers would have to be exposed to contaminated foods over many years for their health to be at risk.

The Food and Drink Federation, which represents Britain's food companies, said the Swiss study was "a good starting point for further investigations" - but not enough in itself to justify discontinuing the use of recycled card.

Manufacturers' reactions

Nonetheless, some of the individual members of the FDF are taking steps to change their packaging.

Kellogg's said it was working with its suppliers on new packaging "which allows us to meet our environmental commitments but will also contain significantly lower levels of mineral oil".

The company is also looking at alternative inner liners for its packets.

Dr Grob's studies suggest only aluminium-coated bags or those made of certain types of thick plastic are an effective barrier to the migration of mineral oils.

Weetabix said it uses 100% recycled board because it is better for the environment, but is also looking at recycled packaging that does not contain recycled newspaper. Like several other companies, it said: "Our data... does indicate that none of our products pose a risk to consumer health".

In Germany the government has told the food and packaging industries to take immediate steps to reduce the risk from mineral oils, and is considering introducing mandatory rules.

In the UK the Food Standards Agency is doing research of its own: but so far it is only looking at how much mineral oil there is in recycled packaging, not how much gets into the food inside.

Terry Donohoe, the acting head of the FSA's chemical safety division, said: "Should there be any evidence from our study - and we will carry out a risk assessment - we will take immediate action to protect the public."

Dr Grob and his colleagues say that even switching to virgin cardboard would not eliminate the risk from mineral oils entirely. This is because food cartons are themselves stored and transported in larger corrugated cardboard boxes which are also made from recycled newspapers, and are also a source of contamination.

http://www.eurekalert.org/pub_releases/2011-03/s-rnb030911.php

Redefining normal blood pressure

Current US definition of 'normal' blood pressure may unnecessarily label 100 million Americans as 'abnormal'

As many as 100 million Americans may currently be misclassified as having abnormal blood pressure, according to Dr. Brent Taylor from the Veterans Affairs Health Care System in Minneapolis and the University of Minnesota and his colleagues. Their findings1 show that these people are not actually more likely to die prematurely than those with 'normal' blood pressure, i.e. below 120/80. Taylor and colleagues' article in the Journal of General Internal Medicine², published by Springer, also shows that in those under 50, diastolic blood pressure* is the more important predictor of mortality, whereas in those over 50, systolic blood pressure* is the stronger predictor. The authors argue it is time to consider a new definition of 'normal' blood pressure.

Taylor and colleagues examined the independent contribution of diastolic blood pressure (DBP) and systolic blood pressure (SBP) on mortality, as well as how these relationships might affect the number of Americans currently labelled as having abnormal blood pressure.

The authors looked at data for 13,792 people from the National Health and Nutrition Examination Survey, which enrolled participants in 1971-76 and followed them up for two decades - they studied DBP, SBP and long-term survival data specifically. In order to assess the underlying distribution of untreated blood pressure in American adults by age, Taylor and team also looked at data for 6,672 adults from the first National Health Examination Survey carried out between 1959 and 1962.

They found that in people aged over 50, those with SBPs above 140, independent of DBP, were significantly more likely to die prematurely. In those aged 50 or less, DBPs above 100 were linked to significant increases in premature death. The authors' analysis offers alternative cut-off points for the definition of 'normal'.

Dr. Taylor concludes: "Our findings highlight that the choice of approach used to define normal blood pressure will impact literally millions of Americans. If we cannot reliably see an effect on mortality in a large group of individuals followed for nearly 20 years, should we define the condition as abnormal? We believe considering this kind of approach represents a critical step in ensuring that diagnoses are given only to those with a meaningful elevation in risk, and targeted towards individuals most likely to benefit."

** Diastolic blood pressure is the lowest pressure within the bloodstream, occurring between heart beats i.e. when the heart relaxes. Systolic blood pressure is the highest pressure within the bloodstream, occurring during each heart beat i.e. when the heart contracts.*

References
1. Taylor BC et al (2011). Impact of diastolic and systolic blood pressure on mortality: implications for the definition of 'normal'. Journal of General Internal Medicine. DOI 10.1007/s11606-011-1660-6
2. The Journal of General Internal Medicine is the official journal of the Society of General Internal Medicine.
http://www.eurekalert.org/pub_releases/2011-03/ru-nsp030911.php

New study proves the brain has 3 layers of working memory

Predictability can improve multitasking

Researchers from Rice University and Georgia Institute of Technology have found support for the theory that the brain has three concentric layers of working memory where it stores readily available items. Memory researchers have long debated whether there are two or three layers and what the capacity and function of each layer is.

In a paper in the March issue of the Journal of Cognitive Psychology, researchers found that short-term memory is made up of three areas: a core focusing on one active item, a surrounding area holding at least three more active items, and a wider region containing passive items that have been tagged for later retrieval or "put on the back burner." But more importantly, they found that the core region, called the focus of attention, has three roles -- not two as proposed by previous researchers. First, this core focus directs attention to the correct item, which is affected by predictability of input pattern. Then it retrieves the item and subsequently, when needed, updates it.

The researchers, Chandramallika Basak of Rice University and Paul Verhaeghen of Georgia Tech, used simple memory tasks involving colors and shapes on a computer screen to determine the three distinct layers of memory. They also determined the roles of attention focus by exploring the process of switching items in and out of the focus of attention.

In their previous studies, Basak and Verhaeghen discovered that response time for switching in and out of the core focus is not affected by the number of items stored when the items are input in a predictable pattern.

In this study of 49 participants across two experiments, the researchers found that when no pattern exists, all participants increased their response time by an average of 240 milliseconds per item as more items are stored. This implies that the area outside the focus has to be searched when there is no pattern, even before the item can be retrieved.

However, as evidenced by the previous studies, when participants were given 10 hours of practice in a memory task with a predictable pattern, all of them could enhance the focus of attention to store four items in the focus core. But this focus does not expand when the memory task has no pattern.

"Predictability can free up resources so a person can effectively multitask," said Basak, assistant professor of psychology at Rice and lead author of the study. "When you do the same sequence over and over again, your memory can be partially automatized so you have the ability to do another task concurrently."

This comes naturally, Basak said. For instance, as you drive the usual route to your regular grocery store, you might also be thinking about what to fix for dinner and making a grocery list. That same secondary task -- the grocery list -- becomes more of a challenge when driving to a different grocery store using an unfamiliar route.

Another facet of the study showed that the third level of memory -- the region containing passive items -- is not only separate from the other two areas of active storage but has a firewall between them. The number of passive items does not influence either response time or accuracy for recalling active items.

http://www.eurekalert.org/pub_releases/2011-03/miot-msi030911.php

MIT scientists identify new H1N1 mutation that could allow virus to spread more easily

In a new study from MIT, researchers have identified a single mutation in the H1N1 genetic makeup that would allow it to be much more easily transmitted between people.

CAMBRIDGE, Mass. -- In the fall of 1917, a new strain of influenza swirled around the globe. At first, it resembled a typical flu epidemic: Most deaths occurred among the elderly, while younger people recovered quickly. However, in the summer of 1918, a deadlier version of the same virus began spreading, with disastrous consequence. In total, the pandemic killed at least 50 million people - about 3 percent of the world's population at the time.

That two-wave pattern is typical of pandemic flu viruses, which is why many scientists worry that the 2009 H1N1 ("swine") flu virus might evolve into a deadlier form.

H1N1, first reported in March 2009 in Mexico, contains a mix of human, swine and avian flu genes, which prompted fears that it could prove deadlier than typical seasonal flu viruses. However, the death toll was much lower than initially feared, in large part because the virus turned out to be relatively inefficient at spreading from person to person.

In a new study from MIT, researchers have identified a single mutation in the H1N1 genetic makeup that would allow it to be much more easily transmitted between people. The finding, reported in the March 2 edition of the journal Public Library of Science (PLoS) One, should give the World Health Organization, which tracks influenza evolution, something to watch out for, says Ram Sasisekharan, senior author of the paper.

"There is a constant need to monitor the evolution of these viruses," says Sasisekharan, the Edward Hood Taplin Professor and director of the Harvard-MIT Division of Health Sciences and Technology. Some new H1N1 strains have already emerged, and the key question, Sasisekharan adds, is whether those strains will have greater ability to infect humans.

WHO labs around the world are collecting samples of human and avian flu strains, whose DNA is sequenced and analyzed for potential significant mutations. However, it's difficult, with current technology, to predict how a particular DNA sequence change will alter the structure of influenza proteins, including hemagglutinin (HA), which binds to receptors displayed by cells in the human respiratory tract. Now that this specific HA mutation has been identified as a potentially dangerous one, the WHO should be able to immediately flag any viruses with that mutation, if they appear.

On June 11, 2009, about three months after the H1N1 virus first appeared, the World Health Organization declared a level 6 pandemic alert (the highest level). Nearly 5,000 H1N1 deaths were reported to the WHO, and more than 400,000 cases were confirmed, though the true number of cases is significantly higher because many countries stopped counting cases after the first few months of the outbreak, according to the WHO.

In July 2009, a team of researchers from MIT, led by Sasisekharan, and the Centers for Disease Control and Prevention reported in the journal Science that the H1N1 virus was much less easily passed from person to person than seasonal flu viruses and earlier pandemic flu viruses such as the second wave of the 1918 strain.

Sasisekharan and CDC senior microbiologist Terrence Tumpey had previously shown that a major factor in flu-virus transmissibility is the structure of the HA protein, which is found on the viral surface. The tightness of fit between HA and the respiratory cell receptor determines how effectively the virus infects a host.

The 2009 H1N1 strain, like the first wave of 1918 (known as the NY18 strain), does not bind efficiently. However, it took only one mutation of the NY18 virus' HA protein to become the much more virulent SC18 strain, which caused the second wave.

In the new PLoS study, the MIT researchers focused on a segment of the HA protein that they have shown affects its ability to bind to respiratory cells. They created a virus with a single mutation in that region, which replaced the amino acid isoleucine with another amino acid, lysine. That switch greatly increased the HA protein's binding strength. They also found that the new virus spread more rapidly in ferrets, which are commonly used to model human influenza infection.

If such a mutant virus evolved, it could generate a "second wave" like the ones seen in 1918 and in 1957 (known as the "Asian flu"). "If you look at the history, it takes a very small change to these viruses to have a dramatic effect," Sasisekharan says.

The amino acid in question is located in a part of the viral genome prone to mutate frequently, because it is near the so-called antigenic site - the part of the HA protein that interacts with human antibodies. Antigenic sites tend to evolve rapidly to escape such antibodies, which is why flu vaccine makers have to use new formulas every year. This year's vaccine included a strain of H1N1, which is still circulating around the world.

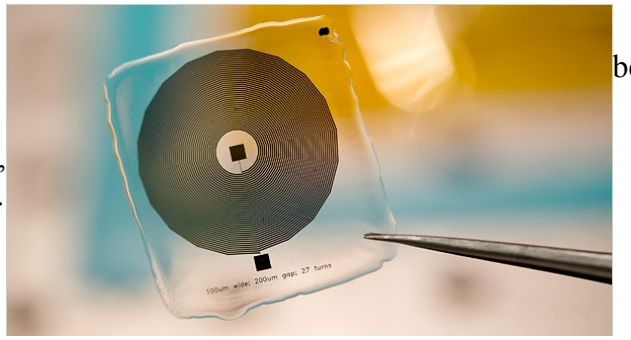
http://www.nytimes.com/2011/03/08/science/08silk.html

The Reinvention of Silk

By HENRY FOUNTAIN

As some silk researchers see it, if spiders were gregarious vegetarians, the world might be a different place.

For spiders are nature's master silk makers, and over millions of years of evolution have developed silks that could be useful to people - from sticky toothpastelike mush to strong and stretchy draglines.



"There's not just one kind of material we're talking about," said Cheryl Hayashi, who studies the evolutionary genetics of spider silk at the University of California, Riverside. "You can look in nature, and there are a lot of solutions already made. You want a glue? There's a silk that's already a glue."

NEW USES Silk creations by Tufts University researchers include a coil made of silk substrate and gold that can help tell when food goes bad. **Bryce Vickmark for The New York Times**

For years there has been talk of the bright promise of spider silk: that it might one day be used to make cables that are stronger than those of steel, for example, or bulletproof vests that are more effective than those made of Kevlar.

There has been a big fly in the ointment, however: spiders cannot spin enough of the stuff. Although a typical spider can produce five types of silk, it does not make much of any of them. Obtaining commercial quantities is a practical impossibility - spiders are loners and require a diet of live insects; some are cannibals. In other words, spider ranching is out of the question.

Researchers have worked to overcome this fundamental limitation by trying to unlock the secrets of the spider's silk-making abilities so silk could be made in the laboratory, or by genetically transferring those abilities to other organisms that could produce silk in quantity. But so far the materials produced lack the full strength, elasticity and other qualities of the real thing.

Some scientists are making an end run around the spider problem and working on reinventing the one silk that is plentiful - that of silkworms. They are reconstituting it to make materials that have the potential to go far beyond the dream of bulletproof vests.

Among these researchers are David Kaplan and others at Tufts University, whose creations have potential applications in medicine and other fields. "Here's a material that's been around for 5,000 years and used in sutures for about that long," Dr. Kaplan said. "Yet there's this untapped territory."

Dr. Kaplan's group and colleagues at the University of Illinois and University of Pennsylvania have recently produced electrode arrays, for example, that are printed on flexible, degradable films of silk. The arrays - so thin they can conform to the nooks and crannies of the surface of the brain - may one day be used to treat epilepsy or other conditions without producing the scarring that larger implanted electrodes do.

For centuries, beginning in China, commercial silk has been produced by cultivating silkworms - the larvae of a moth, Bombyx mori - which, unlike spiders, are content to loll about cheek by jowl, munching on mulberry leaves, spinning the material in quantities large enough to be harvested.

"The advantage of silkworms is that they're easy to grow," Dr. Hayashi said. "They're vegetarians. And they produce silk conveniently in this cocoon. But if you look at a silkworm, it only has one kind of spinneret," she added. "Only one kind of fiber can come out of it. Spiders have this whole toolbox."

Efforts to make analogues of spider silks, however, have resulted in materials that are not much different from other polymers, said David Porter, a scientist at the University of Sheffield in England who works with a group at Oxford that studies the biology of silk making. "The consensus is that almost anybody can make a reasonable silk," Dr. Porter said. "But you really can't differentiate it from a good nylon. To differentiate the natural product, really you've got to get the advantages that nature builds in," he added.

Silk is a fibrous protein, produced in glands within the spider or silkworm and some insects. What these creatures do is something no laboratory has been able to achieve: control the chemistry so exquisitely that the silk, which is a liquid inside the organism, becomes a solid upon leaving it. Chief among the advantages of natural silk is the way the proteins are organized. They are folded in complex ways that help give each silk its unique properties. Scientists have not been able to replicate that intricate folding.

"We're still not getting at the complexity of what's going on in inside an individual spider," Dr. Hayashi said. "There's no lab anywhere in the world where somebody has an artificial silk gland."

Producing spider-silk proteins in other organisms - bacteria, goats, plants and, most recently, silkworms themselves are among those that have been genetically engineered - has limitations because the process of reconstituting the proteins ruins any folding pattern. "As soon as you extract the silk, you basically randomize the protein structure," Dr. Porter said. "You destroy all the capacity of that material to do what it wants."

At Tufts, Dr. Kaplan thinks that eventually, genetically modified plants will produce useful spider-based silk that could be harvested like cotton. Until then, however, he is working with reconstituted silkworm silk, making novel films and other materials.

Dr. Kaplan has been researching silk for 21 years - "sad but true," he joked - and spent much of the first decade learning about the fundamental mechanisms by which silk assembles. "We learned how important water is," he said. "It may sound trivial, but the entire process has been built around controlling water content."

Over the past decade, Dr. Kaplan's group has focused on biomedical applications in fields like tissue engineering. In 2005, a postdoctoral researcher in his laboratory developed a water annealing process, reconstituting the silks slowly in a humid environment. "We got these films that were crystal-clear," Dr. Kaplan said. "No one had ever seen this before with silk."

That led to thoughts about how to make an artificial cornea from silk. But a cornea has to be permeable, so Dr. Kaplan got the idea to involve a laser scientist down the hall, Fiorenzo Omenetto.

“I said, ‘Take it down to Fio and have him poke some holes in it,’ ” Dr. Kaplan recalled. “That led to a whole optical platform based on silk.”

It also led to a long collaboration with Dr. Omenetto, who has developed ways to pattern silk films, making diffraction gratings and other structures. The grating can act as a substrate for other proteins or compounds, raising the possibility that silk films could be used for implantable biosensors or in drug delivery, with the silk dissolving in the body at a controlled rate to release the drug.

One advantage with silk, Dr. Omenetto said, is that the process of making films or other structures is “green” - water-based and at low temperatures. “You can make incredibly sophisticated diffraction gratings out of glass or plastic,” he said. “But those are made at high temperatures or in a very harsh chemical environment,” conditions that would make it difficult to incorporate drugs or other compounds.

Researchers elsewhere have further developed the idea of using silk films for medical applications. At the Georgia Institute of Technology, Eugenia Kharlampieva experimented with depositing silver nanoparticles on films of silk as a way of strengthening them. “Silk is a wonderful material because it’s biocompatible,” said Dr. Kharlampieva, who is continuing her research at the University of Alabama, Birmingham. “The main drawback is it’s soft. If you want to use it for optical applications, you need to reinforce it.”

The films she uses are extremely thin, and she layers them. “We make this nanocomposite which is flexible, still soft, but mechanically stronger.” Because the films remain flexible, Dr. Kharlampieva is experimenting with fashioning them into tiny capsules that could contain minute quantities of drugs. Potentially as small as blood cells, they could be used to deliver drugs through the bloodstream.

At Tufts, Dr. Omenetto’s work on patterning silk has led to even more exotic potential applications. Among the latest, developed with colleagues at Boston University, is the idea of using silk as the basis for metamaterials, which can manipulate light or other electromagnetic radiation in ways that nature ordinarily cannot. By producing intricate structures in the films and depositing metal on them, metamaterial antennas may be produced that could be used inside the body as a means of monitoring health - the signal from the antenna changing as conditions inside the body change.

Such applications may be far off, Dr. Omenetto said, but the potential is vast - a fact he realized when he was first asked to poke holes in silk. “It looked like a cool optical material,” he said. “And I haven’t been sleeping that much ever since.”

This article has been revised to reflect the following correction:

Correction: March 7, 2011 *An earlier version of this article misstated the academic affiliation of David Porter. He is with the University of Sheffield, not Suffield University.*

http://www.eurekalert.org/pub_releases/2011-03/sumc-ssd030711.php

Stanford scientists discover anti-anxiety circuit in brain region considered the seat of fear

STANFORD, Calif. - ***Stimulation of a distinct brain circuit that lies within a brain structure typically associated with fearfulness produces the opposite effect: Its activity, instead of triggering or increasing anxiety, counters it.***

That's the finding in a paper by Stanford University School of Medicine researchers to be published online March 9 in Nature. In the study, Karl Deisseroth, MD, PhD, and his colleagues employed a mouse model to show that stimulating activity exclusively in this circuit enhances animals' willingness to take risks, while inhibiting its activity renders them more risk-averse. This discovery could lead to new treatments for anxiety disorders, said Deisseroth, an associate professor of bioengineering and of psychiatry and behavioral science.

The investigators were able to pinpoint this particular circuit only by working with a state-of-the-art technology called optogenetics, pioneered by Deisseroth at Stanford, which allows brain scientists to tease apart the complex circuits that compose the brain so these can be studied one by one.

"Anxiety is a poorly understood but common psychiatric disease," said Deisseroth, who is also a practicing psychiatrist. More than one in four people, in the course of their lives, experience bouts of anxiety symptoms sufficiently enduring and intense to be classified as a full-blown psychiatric disorder. In addition, anxiety is a significant contributing factor in other major psychiatric disorders from depression to alcohol dependence, Deisseroth said.

Most current anti-anxiety medications work by suppressing activity in the brain circuitry that generates anxiety or increases anxiety levels. Many of these drugs are not very effective, and those that are have significant side effects such as addiction or respiratory suppression, Deisseroth said. "The discovery of a novel circuit whose action is to reduce anxiety, rather than increase it, could point to an entire strategy of anti-anxiety treatment," he added.

Ironically, the anti-anxiety circuit is nestled within a brain structure, the amygdala, long known to be associated with fear. Generally, stimulating nervous activity in the amygdala is best known to heighten anxiety. So the anti-anxiety circuit probably would have been difficult if not impossible to locate had it not been for optogenetics, a new technology in which nerve cells in living animals are rendered photosensitive so that action in these cells can be turned on or off by different wavelengths of light. The technique allows researchers to selectively photosensitize particular sets of nerve cells. Moreover, by delivering pulses of light via optical fibers to specific brain areas, scientists can target not only particular nerve-cell types but also particular cell-to-cell connections or nervous pathways leading from one brain region to another. The fiber-optic hookup is both flexible and pain-free, so experimental animals' actual behavior as well as their brain activity can be monitored.

In contrast, older research approaches involve probing brain areas with electrodes to stimulate nerve cell firing. But an electrode stimulates not only all the nerve cells that happen to be in the neighborhood but even fibers that are just passing through on the way to somewhere else. Thus, any effect from stimulating the newly discovered anti-anxiety circuit would have been swamped by the anxiety-increasing effects of the dominant surrounding circuitry.

In December 2010, the journal Nature Methods bestowed its "Method of the Year" title on optogenetics.

In the new Nature study, the researchers photosensitized a set of fibers projecting from cells in one nervous "switchboard" to another one within the amygdala. By carefully positioning their light-delivery system, they were able to selectively target this projection, so that it alone was activated when light was pulsed into the mice's brains. Doing so led instantaneously to dramatic changes in the animals' behavior.

"The mice suddenly became much more comfortable in situations they would ordinarily perceive as dangerous and, therefore, be quite anxious in," said Deisseroth. For example, rodents ordinarily try to avoid wide-open spaces such as fields, because such places leave them exposed to predators. But in a standard setup simulating both open and covered areas, the mice's willingness to explore the open areas increased profoundly as soon as light was pulsed into the novel brain circuit. Pulsing that same circuit with a different, inhibitory frequency of light produced the opposite result: the mice instantly became more anxious. "They just hunkered down" in the relatively secluded areas of the test scenario, Deisseroth said.

Standard laboratory gauges of electrical activity in specific areas of the mice's amygdalas confirmed that the novel circuit's activation tracked the animals' increased risk-taking propensity.

Deisseroth said he believes his team's findings in mice will apply to humans as well. "We know that the amygdala is structured similarly in mice and humans," he said. And just over a year ago a Stanford team led by Deisseroth's associate, Amit Etkin, MD, PhD, assistant professor of psychiatry and behavioral science, used functional imaging techniques to show that human beings suffering from generalized anxiety disorder had altered connectivity in the same brain regions within the amygdala that Deisseroth's group has implicated optogenetically in mice.

The study was funded by the National Institutes of Health, the National Institute of Mental Health, the National Institute on Drug Abuse, the National Science Foundation, NARSAD, a Samsung Scholarship, and the McKnight, Woo, Snyder, and Yu foundations. Kay Tye, PhD, a postdoctoral researcher in the Deisseroth laboratory, and Rohit Prakash, Sung-Yon Kim and Lief Fenno, all graduate students in that lab, shared first authorship. Other co-authors are graduate student Logan Grosenick, undergraduate student Hosniya Zarabi, postdoctoral researcher Kimberly Thompson, PhD, and research associates Viviana Gradinaru and Charu Ramakrishnan, all of the Deisseroth lab.

Stanford has filed for intellectual property protection to ensure free and unfettered use for research, and Deisseroth and his colleagues have no financial interest in the outcome of their work.

http://www.eurekalert.org/pub_releases/2011-03/sumc-dim030711.php

Differences in mammalian brain structure and genitalia linked to specific DNA regions in new study

STANFORD, Calif. - ***Humans are clearly different from chimpanzees. The question is, why? According to researchers at the Stanford University School of Medicine, it may boil down in part to what we don't have, rather than what we do.***

The loss of snippets of regulatory DNA, the scientists found, could be the reason why, for example, humans lack the penile spines found in many other mammals, and also why specific regions of our brains are larger than those of our closest relatives.

Understanding these and other differences may help us learn what it means to be human. But it took the recent advent of whole-genome sequencing of several species and an open-minded, combined computational and experimental approach to reveal the particular two-steps-forward, one-step-back evolutionary dance that set us apart from other primates millions of years ago.

"Rather than looking for species-specific differences in specific genes or genomic regions that exist in humans, we asked, 'Are there functional, highly conserved genetic elements in the chimpanzee genome that are

completely missing in humans?"' said Gill Bejerano, PhD, assistant professor of developmental biology and of computer science. "We found several hundred locations that, as far as we could see, are absent in our species alone." Until now, many evolutionary geneticists focused on differences among genes, rather than the regulatory regions outside the genes.

Losing small pieces of regulatory DNA, rather than the genes they control, means that the related changes are likely to be subtle: Although the location or the timing of the expression of the gene within the body may change, the gene product itself remains functional. The distinction leads to viable differences among individuals that can eventually lead to the development of new traits and species.

"It's not only unusual, but also particularly interesting, to find these sequences missing in humans," said David Kingsley, PhD, professor of developmental biology. "These are the same type of molecular events that have been shown to produce evolutionary differences among other organisms."

Other organisms like the three-spined stickleback fish, for instance. Kingsley's previous research focused on understanding how similar genetic changes over time have led to body modifications in the small fish that allow it to live in many very different environments.

"In fish, we find that the loss of regulatory DNA has produced key evolutionary differences in body structures," Kingsley said. "The current study not only identifies an intriguing list of deletions in humans, but also links particular deletions with specific anatomical changes that are unique to the human lineage."

Bejerano and Kingsley are co-senior authors of the research, which will be published March 10 in Nature. Three scientists share first authorship of the article: Cory McLean, a graduate student in Bejerano's laboratory; Alex Pollen, a graduate student in Kingsley's laboratory; and Philip Reno, PhD, a former postdoctoral scholar in Kingsley's laboratory now starting his own lab at Pennsylvania State University.

The researchers compared the genomes of several species to identify 510 regions that are highly conserved among chimpanzees and other mammals but are missing in humans. (Only one of the regions contained a coding region of a gene, or the portion that is turned into proteins to do the cell's work.) They then used a software program developed in Bejerano's laboratory called GREAT (for genomic regions of enrichment of annotations tool) to see whether these regions preferentially occurred near certain types of genes. (GREAT is publicly available to researchers around the world at http://great.stanford.edu.)

"We basically asked where evolution favored tweaking gene expression to get human-specific traits," said Bejerano. "We found two main categories of enrichment: genes involved in receptor signaling for steroid hormones like testosterone, and genes involved in neural development in the brain."

"Most, but not all, of these regions are also missing in the Neanderthal genome," said Kingsley, "which indicates the deletion took place more than 500,000 years ago."

The researchers found that one of the missing regions normally drives the expression of the androgen receptor in sensory whiskers and genitalia. Androgen is a sex hormone responsible for growth of sensory hairs, or vibrissae, and surface spines found on the penises of many mammals. The loss of these structures in humans decreases tactile sensitivity and increases the duration of intercourse in humans relative to other species. Another region was adjacent to a tumor suppressor gene that suppresses neural growth in a particular part of the brain. Loss of expression of this inhibitory gene could thus contribute to an expansion of neural production in humans and a larger brain. The resulting changes may have paved the way for monogamous pair-bonding and the complex social structure necessary to raise our species' relatively helpless infants, the scientists speculate.

There are still many other human-specific deletions to investigate, say the scientists, who are encouraging their lab members to study the functions of other interesting regions.

"Finding these sorts of human-specific changes is also a good motivator to look at other genomic events," said Bejerano. "Previous work in my lab has shown that many thousands of DNA regions are highly conserved among mammals, and almost never lost during evolution. Much of my lab is devoted to understanding what these regions do. Now we are starting to learn what can happen when they are lost."

The work was supported by a Stanford Bio-X graduate fellowship, a Ruth L. Kirschstein National Research Service Award, a National Defense Science and Engineering graduate fellowship, a National Science Scholarship of the Agency of Science, Technology and Research, a Stanford graduate fellowship, the National Institutes of Health, the Edward Mallinckrodt, Jr. Foundation and the Howard Hughes Medical Institute.

http://news.discovery.com/space/very-cold-brown-dwarf-discovered-110309.html

Record Breaker: 'Very Cold' Brown Dwarf Discovered

By Ian O'Neill | Wed Mar 9, 2011 05:34 AM ET

A brown dwarf, about 75 light-years from Earth, has hit a new low. In fact, its temperature is so low that it is about the same temperature as the cup of tea sitting at my desk. Ladies and gentlemen, meet "CFBDSIR J1458+1013B," the sub-100 degree Celsius (212 F) failed star.*

A group of astronomers headed by Michael Liu, of the University of Hawaii, used the awesome power of adaptive optics on the 10-meter Keck II Telescope on Mauna Kea to probe the very faint infrared signature of this brown dwarf -- which exists as a brown dwarf binary, orbiting with its partner, CFBDSIR J1458+1013A -- revealing that the object may belong to a notoriously rare type of brown dwarf. This object is the faintest brown dwarf spotted by far and it is estimated to be only 6-15 times the mass of Jupiter.

Brown Dwarfs = Stellar Failures?

You may have heard brown dwarfs being referred to as "failed stars" as they are not massive enough to support nuclear fusion in their cores, and yet they can't be called "planets" as they don't exhibit chemical differentiation with depth and have convective flows -- a very star-like quality. Therefore, they exist in a stellar hinterland, where they are neither a star or a planet, and yet exhibit characteristics of both.

But astronomers still classify brown dwarfs by their spectral type (a scale of letters assigned to the luminosity of stars), which relates to their temperature. At the lowest, coolest end of the scale, radiating in infrared wavelengths, are the oddball brown dwarfs.

So far, the coolest brown dwarfs observed exist at the lowest end of the scale, with a spectral class of "T." However, there is a theoretical class "Y" that is even cooler than the T-class brown dwarfs -- they are predicted to have a temperature less than 225 degrees Celsius (440 F).

More Like a Planet? More Like a Star?

Although Y-class candidates have been spotted by other instruments, the Keck telescope has put a very tight constraint on the temperature of CFBDSIR J1458+1013B and it looks as if this brown dwarf has more "planet-like" qualities than "star-like" qualities, with a temperature of 97 degrees Celsius (give or take 40 degrees C).

Could CFBDSIR J1458+1013B be the missing link between stars and planets? How can we work out if this object is more like Jupiter, say, or more like the sun?

Usually, water will exist in a gaseous state in brown dwarf atmospheres. But at such low temperatures, it is expected that water in the brown dwarf's atmosphere will condense to form clouds. Although it is hard to detect condensing water in this brown dwarf's atmosphere, it is certainly a prime "Y" class candidate.

Regardless, CFBDSIR J1458+1013B is the coolest brown dwarf in the cosmic neighborhood and it could help us understand the point at which a star becomes a star and a planet becomes a planet.

**Although brown dwarfs are known as "failed stars," I like to refer to them as "overachieving planets." Whoever said that becoming a star was the pinnacle of stellar living anyway?*

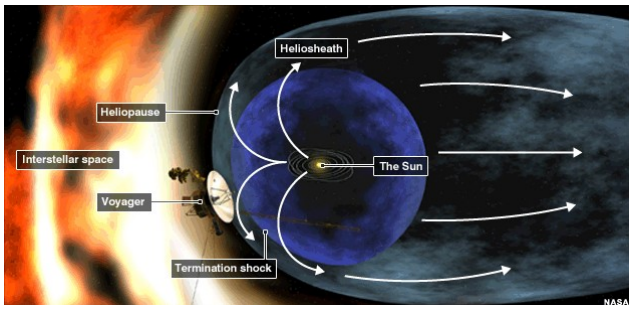
Publication: "CFBDSIR J1458+1013B: A Very Cold (>T10) Brown Dwarf in a Binary System," Liu et al., 2011, arXiv:1103.0014v2 [astro-ph.SR]

http://www.bbc.co.uk/news/science-environment-12688246

Voyager: Still dancing 17 billion km from Earth

By Jonathan Amos Science correspondent, BBC News

The extraordinary Voyager 1 spacecraft is demonstrating its nimbleness more than 30 years after leaving Earth.



At the astonishing distance of 17.4 billion km, the Nasa probe is the most far-flung object made by humans. But it seems age and remoteness are no barriers to this veteran explorer.

Voyager is executing a series of roll manoeuvres to get one of its instruments into the optimum position to measure particles sweeping away from the Sun. Controllers at the US space agency's Jet Propulsion Laboratory in Pasadena, California, report a perfect response from the probe.

Nasa Voyager is approaching the edge of the bubble of charged particles the Sun has thrown out into space

"I liken Voyager to an old car," said project manager Suzanne Dodds. "It's got simple electronics, not a lot of fancy gadgets - but because of that it can operate for longer; it's not as finicky."

Voyager 1 was launched in 1977 on a tour of the outer planets. Since completing that mission, it has been making the push for deep space. The probe is heading in the general direction of the centre of our Milky Way Galaxy and will, in the next few years, leave the space dominated by the influence of our Sun and enter the province between the stars - interstellar space.

Scientists know that to be the case because of the way the solar wind is behaving at Voyager's current location.

This stream of charged particles forms a bubble around our Solar System known as the heliosphere. The wind travels at "supersonic" speed until it crosses a shockwave called the termination shock.

At this point, the wind then slows dramatically and heats up in a region termed the heliosheath. Voyager has determined the velocity of the wind at its location has now slowed to zero. Very simply put, Voyager has reached the domain where the solar wind is starting to turn back on itself as it pushes up against the particles of interstellar space.

The new manoeuvres are designed to enable Voyager 1's Low Energy Charged Particle (LECP) instrument to investigate precisely what is going on around it. "It counts the particles and measures their direction," explained Suzanne Dodds. "This will give us a much better picture of what's happening with the solar wind close to the heliopause (the "official" edge of the Solar System). It could be that as we do these measures we see its direction change. All we have out there is models and every time we get data the models don't quite fit what Voyager sees, and then we have to update the models."

On Monday this week Voyager rolled 70 degrees anticlockwise as seen from Earth from its normal orientation. It held the position by spinning gyroscopes for two hours, 33 minutes. The veteran last performed such a manoeuvre in 1990 when it took pictures of the planets it was leaving behind.

Once complete, Voyager rolled back and locked on to its guide star, Alpha Centauri.

Voyager 1 will do more roll-and-holds this week, and if the spacecraft continues to function well it will execute a series of weekly rolls to gather particle data every three months.

The Voyager 2 spacecraft which was also launched in 1977 is not quite as far from Earth. It is a mere 14 billion kilometres away. At these great distances, communication with the probes is a lengthy business. The one-way travel time for a radio message to get to Voyager 1 is now 16 hours.

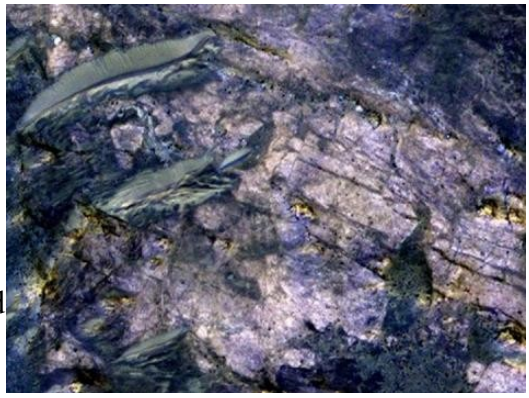
Suzanne Dodds commented: "People love Voyager I think because the mission has lasted so long. We're still talking to it and it's just so far out in space; people have a real attachment to it. It did its grand tour past the planets and it just goes on, on this voyage of discovery."

http://www.physorg.com/news/2011-03-mars-carbon-dioxide.html

Mars' missing carbon dioxide may be buried

(PhysOrg.com) -- ***Rocks on Mars dug from far underground by crater-blasting impacts are providing glimpses of one possible way Mars' atmosphere has become much less dense than it used to be.***

At several places where cratering has exposed material from depths of about 5 kilometers (3 miles) or more beneath the surface, observations by a mineral-mapping instrument on NASA's Mars Reconnaissance Orbiter indicate carbonate minerals.



These are not the first detections of carbonates on Mars. However, compared to earlier findings, they bear closer resemblance to what some scientists have theorized for decades about the whereabouts of Mars' "missing" carbon. If deeply buried carbonate layers are found to be widespread, they would help answer questions about the disappearance of most of ancient Mars' atmosphere, which is deduced to have been thick and mostly carbon dioxide. The carbon that goes into formation of carbonate minerals can come from atmospheric carbon dioxide.

This image from orbit covers an area about 460 meters (about 1,500 feet) across, in which carbonate minerals have been identified from spectrometer observations. Fractures and possible layers are visible in the light-toned rock exposure containing the carbonates. **Credit: NASA/JPL-Caltech/Univ. of Arizona**

"We're looking at a pretty lucky location in terms of exposing something that was deep beneath the surface," said planetary scientist James Wray of Cornell University, Ithaca, N.Y., who reported the latest carbonate findings today at the Lunar and Planetary Science Conference near Houston. Huygens crater, a basin 467 kilometers (290 miles) in diameter in the southern highlands of Mars, had already hoisted material from far underground, and then the rim of Huygens, containing the lifted material, was drilled into by a smaller, unnamed cratering event.

Observations in the high-resolution mode of the Compact Reconnaissance Imaging Spectrometer for Mars (CRISM) instrument on the Mars Reconnaissance Orbiter show spectral characteristics of calcium or iron carbonate at this site. Detections of clay minerals in lower-resolution mapping mode by CRISM had prompted closer examination with the spectrometer, and the carbonates are found near the clay minerals. Both types of minerals typically form in wet environments.

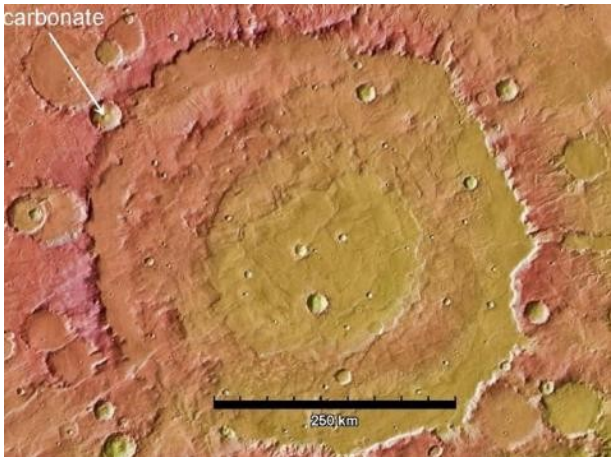
The occurrence of this type of carbonate in association with the largest impact features suggests that it was buried by a few kilometers (or miles) of younger rocks, possibly including volcanic flows and fragmented material ejected from other, nearby impacts.

These findings reinforce a report by other researchers five months ago identifying the same types of carbonate and clay minerals from CRISM observation of a site about 1,000 kilometers (600 miles) away. At that site, a meteor impact has exposed rocks from deep underground, inside Leighton crater. In their report of that discovery, Joseph Michalski of the Planetary Science Institute, Tucson, Ariz., and Paul Niles of NASA Johnson Space Center, Houston, proposed that the carbonates at Leighton "might be only a small part of a much more extensive ancient sedimentary record that has been buried by volcanic resurfacing and impact ejecta."

Carbonates found in rocks elsewhere on Mars, from orbit and by NASA's Spirit rover, are rich in magnesium. Those could form from reaction of volcanic deposits with moisture, Wray said. "The broader compositional range we're seeing that includes iron-rich and calcium-rich carbonates couldn't form as easily from just a little bit of water reacting with igneous rocks. Calcium carbonate is what you typically find on Earth's ocean and lake floors."

He said the carbonates at Huygens and Leighton "fit what would be expected from atmospheric carbon dioxide interacting with ancient bodies of water on Mars." Key additional evidence would be to find similar deposits in other regions of Mars. A hunting guide for that search is the CRISM low-resolution mapping, which has covered about three-fourths of the planet and revealed clay-mineral deposits at thousands of locations.

"A dramatic change in atmospheric density remains one of the most intriguing possibilities about early Mars," said Mars Reconnaissance Orbiter Project Scientist Richard Zurek, of NASA's Jet Propulsion Laboratory, Pasadena, Calif. "Increasing evidence for liquid water on the surface of ancient Mars for extended periods continues to suggest that the atmosphere used to be much thicker."



This image shows the context for orbital observations of exposed rocks that had been buried an estimated 5 kilometers (3 miles) deep on Mars. **Credit: NASA/JPL-Caltech/Univ. of Arizona**

Carbon dioxide makes up nearly all of today's Martian air and likely was most of a thicker early atmosphere, too. In today's thin, cold atmosphere, liquid water quickly freezes or boils away.

What became of that carbon dioxide? NASA will launch the Mars Atmosphere and Volatile Evolution Mission (MAVEN) in 2013 to investigate processes that could have stripped the gas from the top of the atmosphere into interplanetary space. Meanwhile, CRISM and other instruments now in orbit continue to look for evidence that some of the carbon dioxide in that ancient atmosphere was removed, in the presence of liquid water, by formation of carbonate minerals now buried far beneath the present surface. *Provided by JPL/NASA*

http://www.eurekalert.org/pub_releases/2011-03/ctco-bcr031011.php

Brain cell regrowth linked to benefits of exercise, sexual behaviors and reproductive issues

Two studies link the regrowth of key adult brain cells in two critical areas of the brain to both the benefits of exercise as a stress reducer and also to sexual behavior and reproductive issues

Tampa, Fla. – Two studies published by an interdisciplinary team of Hong Kong researchers in the current special issue of Cell Transplantation (20:1), ***now freely available on-line***, link the regrowth of key adult brain cells (neurogenesis) in two critical areas of the brain to both the benefits of exercise as a stress reducer and also to sexual behavior and reproductive issues. The two studies reviewing the causes and impacts of neurogenesis came out of a recent Pan Pacific Symposium on Stem Cell Research held in Taichung, Taiwan.

Until the 1960s, the idea that the adult brain could experience neural cell re-growth was not accepted; research over the next 30 years confirmed that adult brain cells could, and did, in fact, regenerate. Recent research has focused on the role of neurogenesis. Subsequent important findings promise to change not only therapeutic interventions, but our understanding of aging, sexual potency and psychiatric diseases as well.

"The discovery of neural stem cells in the adult brain was a spectacular event that revolutionized the traditional view that the central nervous system did not generate new neurons in adulthood," said corresponding author Dr. Kwok-Fai So of the University of Hong Kong in the People's Republic of China. "Our research is focused on questions about the function and physiological significance of neurogenesis and what factors promote or suppress neurogenesis."

Physical exercise may counteract stress by promoting neurogenesis

"**The beneficial effects** of running correlated with increased adult neurogenesis, which may provide a hint that newborn neurons could be involved in counteracting stress-related disorders," said Dr. So. "Research has

shown that exercise can improve mood and cognition and has also demonstrated that a deficit in adult neurogenesis may result in depressive disorders. Our research is aimed at examining the relationship between exercise as a way of combating stress and the possibility that exercise may promote neurogenesis and that neurogenesis functions as the mechanism of benefit."

According to the researchers, one important adult brain area that is a 'neurogenic zone' is the hippocampus, an area involved in memory and emotional regulation. The role of new neurons in hippocampal functions "remains poorly defined," however, but they add that the effect of stress on the hippocampus is well known. Stress, especially depression and post-traumatic brain injury, have been shown to shrink the hippocampus. Recent research has shown that exercise has a link to enhancing hippocampal 'plasticity' and the regrowth of neurons – neurogenesis.

"Recent findings suggest that hippocampal neurogenesis plays a role in the beneficial effects of exercise in countering stress," they concluded.

Citation: Yau, S-K.; Lau, B. W-M.; So, K-F. Adult Hippocampal Neurogenesis: A Possible Way How Physical Exercise Counteracts Stress. Cell Transplantation 20(1):99-111; 2011.

Adult neurogenesis, reproduction and sexual behavior According to the researchers, recent studies suggest adult neurogenesis in the brain's subventricular zone (SVZ), which lines the ventricles (cavities) of the brain that contain cerebrospinal fluid, plays a role in reproductive function and possibly in maternal behaviors, although the function of "SVZ neurogenesis is obscure." They suggest that emerging evidence points to reproductive action and sexual cues, such as pheromones (known to play an important role in reproductive function), may play a role in regulating neurogenesis in the olfactory system, where the sense of smell is located, and in the SVZ. The precise contribution of newborn neurons to sexual behavior is still "under debate," the researchers point out. They cite animal studies showing that neurogenesis plays a role in female mate selection and that suppressed neurogenesis has been associated with decreased sexual performance.

"The potential importance of neurogenesis in sexual behavior, sexual cues and reproductive function has provided new insights," said Dr. So. "These insights might provide a better understanding of sexual dysfunction, sexual disorders and normal sexual functioning."

"These reviews show that the process of neurogenesis has far-reaching implications, including a beneficial exercise-induced response to stress and some degree of involvement with sexual behavior and reproduction," said Prof. Shinn-Zong Lin, professor of neurosurgery at China University Medical Hospital, Taiwan and chair of the Pan Pacific Symposium on Stem Cell Research where this work was first presented. "The studies reinforce the importance of a naturally occurring process that, until recently, was believed to be impossible."

Citation: Lau, B. W-M.; Yau, S-Y.; So, K-F. Reproduction: A New Venue for Studying Function of Adult Neurogenesis? Cell Transplantation 20(1):21-35; 2011.

http://www.eurekalert.org/pub_releases/2011-03/msu-gtl031011.php

Grab the leash: Dog walkers more likely to reach exercise benchmarks

Promoting dog ownership could lead to healthier adults

EAST LANSING, Mich. - Man's best friend may provide more than just faithful companionship: A new study led by a Michigan State University researcher shows people who owned and walked their dogs were 34 percent more likely to meet federal benchmarks on physical activity.

The results, said epidemiologist Mathew Reeves, show that promoting dog ownership and dog walking could help many Americans – of which fewer than half meet recommended levels of leisure-time physical activity – become healthier. "Walking is the most accessible form of physical activity available to people," Reeves said. "What we wanted to know was if dog owners who walked their dogs were getting more physical activity or if the dog-walking was simply a substitute for other forms of activity."

The study appears in the current issue of the Journal of Physical Activity and Health.

Using data from the Michigan Behavioral Risk Factor Survey, an annual health survey conducted by the Centers for Disease Control and Prevention and the Michigan Department of Community Health, Reeves and his team found that not only did owning and walking a dog impact the amount of walking a person does but also that dog walkers were more active overall. The study showed people who walked their dogs generally walked about an hour longer per week than people who owned dogs but did not walk them.

"Obviously you would expect dog walkers to walk more, but we found people who walked their dog also had higher overall levels of both moderate and vigorous physical activities," he said. "There appears to be a strong link between owning and walking a dog and achieving higher levels of physical activity, even after accounting for the actual dog walking."

The study analyzed the amount of leisure-time physical activity a person gets; examples include sports participation, exercise conditioning and recreational activities such as walking, dancing and gardening. Public

health benchmarks call for at least 150 minutes of such activity a week. "There is no magic bullet in getting people to reach those benchmarks," Reeves said. "But owning and walking a dog has a measurable impact."

He also pointed out the social and human/animal bond aspects of owning a dog that has been shown to have a positive impact on quality of life. And since only about two-thirds of dog owners reported regularly walking their dogs, Reeves said dog ownership represents a opportunity to increase participation in walking and overall physical activity.

"The findings suggest public health campaigns that promote the responsible ownership of a dog along with the promotion of dog walking may represent a logical opportunity to increase physical activity," he said.

Other findings in the study revealed: Middle-age people have the least amount of time to walk their dogs; younger and older people get the most physical activity benefit; dogs 1 year old or younger were more likely to be walked than older dogs; and larger breed dogs (those more than 45 pounds) were walked for a longer duration than smaller dogs.

The study can be found at http://journals.humankinetics.com/jpah-current-issue. Contributing authors to the research include Ann Rafferty, Corinne Miller and Sarah Lyon-Callo, all with the Michigan Department of Community Health.

http://www.eurekalert.org/pub_releases/2011-03/du-arg030711.php

Aging rates, gender gap in mortality similar across all primates

DURHAM, N.C. -- ***Humans aren't the only ones who grow old gracefully, says a new study of primate aging patterns.***

For a long time it was thought that humans, with our relatively long life spans and access to modern medicine, aged more slowly than other animals. Early comparisons with rats, mice, and other short-lived creatures confirmed the hunch. But now, the first-ever multi-species comparison of human aging patterns with those in chimps, gorillas, and other primates suggests the pace of human aging may not be so unique after all.

The findings appear in the March 11 issue of Science.

You don't need to read obituaries or sell life insurance to know that death and disease become more common as we transition from middle age to old age. But scientists studying creatures from mice to fruit flies long assumed the aging clock ticked more slowly for humans.

We had good reason to think human aging was unique, said co-author Anne Bronikowski, an associate professor at Iowa State University. For one, humans live longer than many animals. There are some exceptions - parrots, seabirds, clams and tortoises can all outlive us - but humans stand out as the longest-lived primates.

"Humans live for many more years past our reproductive prime," Bronikowski said. "If we were like other mammals, we would start dying fairly rapidly after we reach mid-life. But we don't," she said. "There's been this argument in the scientific literature for a long time that human aging was unique, but we didn't have data on aging in wild primates besides chimps until recently," said co-author Susan Alberts, associate director at the NSF-funded National Evolutionary Synthesis Center in Durham, N.C., and a biologist at Duke University.

The researchers combined data from long-term studies of seven species of wild primates: capuchin monkeys from Costa Rica, muriqui monkeys from Brazil, baboons and blue monkeys from Kenya, chimpanzees from Tanzania, gorillas from Rwanda, and sifaka lemurs from Madagascar.

The team focused not on the inevitable decline in health or fertility that come with advancing age, but rather on the risk of dying. When they compared human aging rates - measured as the rate at which mortality risk increases with age - to similar data for nearly 3,000 individual monkeys, apes and lemurs, the human data fell neatly within the primate continuum.

"Human patterns are not strikingly different, even though wild primates experience sources of mortality from which humans may be protected," the authors wrote in a letter to Science.

The results also confirm a pattern observed in humans and elsewhere in the animal kingdom: as males age, they die sooner than their female counterparts. In primates, the mortality gap between males and females is narrowest for the species with the least amount of male-male aggression - a monkey called the muriqui - the researchers report.

"Muriquis are the only species in our sample in which males do not compete overtly with one another for access to mates," said co-author Karen Strier, an anthropologist at the University of Wisconsin who has studied muriquis since 1982. The results suggest the reason why males of other species die faster than females may be the stress and strain of competition, the authors said.

Do the findings have any practical implications for humans? Modern medicine is helping humans live longer than ever before, the researchers note.

"Yet we still don't know what governs maximum life span," Alberts said. "Some human studies suggest we might be able to live a lot longer than we do now. Looking to other primates to understand where we are and aren't flexible in our aging will help answer that question."

CITATION: *Bronikowski, A., J. Altmann, et al. (2011). "Aging in the natural world: comparative data reveal similar mortality patterns across primates." Science 331(6022).*

Study authors (in alphabetical order) and their areas of expertise are:	*Linda Fedigan (University of Calgary) - capuchin monkeys, Costa Rica*
Susan Alberts (Duke University) - baboons, Kenya	*Anne Bronikowski (Iowa State University) - demography and life history*
Anne Pusey (Duke University) - chimpanzees, Tanzania	*Karen Strier (University of Wisconsin-Madison) - muriqui monkeys, Brazil*
Jeanne Altmann (Princeton University) - baboons, Kenya	*Diane Brockman (University of North Carolina-Charlotte) - lemurs, Madagascar*
Marina Cords (Columbia University) - blue monkeys, Kenya	*Tara Stoinski (Dian Fossey Gorilla Fund International and Zoo Atlanta) - gorillas, Rwanda*
William Morris (Duke University) - demographic and ecological analysis	*Study data are available in the Dryad Digital Repository at http://datadryad.org/handle/10255/dryad.8682.*

http://www.eurekalert.org/pub_releases/2011-03/aha-cdl030711.php

Coffee drinking linked to reduced stroke risk in women

American Heart Association rapid access journal report

Drinking more than a cup of coffee a day was associated with a 22 percent to 25 percent lower risk of stroke, compared with those who drank less, in a study reported in Stroke: Journal of the American Heart Association.

Low or no coffee consumption was associated with an increased risk of stroke in a study of 34,670 women (ages 49 to 83) followed for an average 10.4 years. It's too soon to change coffee-drinking habits, but the study should ease the concerns of some women, researchers noted.

Coffee is one of the most widely consumed beverages in the world. "Therefore, even small health effects of substances in coffee may have large public health consequences," said Susanna Larsson, Ph.D., lead author of the study and a researcher in the Division of Nutritional Epidemiology, National Institute of Environmental Medicine, Karolinska Institute in Stockholm, Sweden.

Groups who reported drinking 1-2 cups per day, 3-4 cups per day or 5 or more cups per day had similar benefits compared with those who reported daily intake of less than a cup of coffee, researchers said. The differences were unchanged by smoking status, body mass index, history of diabetes, hypertension or alcohol consumption, indicating that coffee's effects are not influenced by those known cardiovascular risk factors.

Scientists have theorized that coffee could have either beneficial or harmful effects on the cardiovascular system, but earlier studies have been inconclusive. Only one previous prospective study, which was also inconclusive, examined the association between coffee consumption and stroke incidence in healthy women.

"Our research group has previously observed an inverse association between coffee consumption and risk in Finnish male smokers," Larsson said. "We wanted to assess the situation in women."

The women participated in the long-running Swedish Mammography Cohort, an epidemiological study investigating the association between diet, lifestyle and disease development. All the women were free of cardiovascular disease and cancer at baseline in 1997, when they answered the food frequency questionnaire analyzed in the study. Researchers collected data on cases of first stroke that occurred between Jan. 1, 1998 and Dec. 31, 2008, by linking the study group with the Swedish Hospital Discharge Registry that provides almost complete coverage of Swedish hospital discharges.

Researchers documented 1,680 strokes: 1,310 cerebral infarctions/ischemic strokes (caused by blockages), 154 intracerebral hemorrhages (caused by bleeding inside the brain), 79 subarachnoid hemorrhages (caused by bleeding on the surface of the brain) and 137 unspecified strokes.

After adjustment for other risk factors, coffee consumption was associated with a statistically significant lower risk of total stroke, cerebral infarction and subarachnoid hemorrhage, Larsson said.

The small numbers of intracerebral hemorrhage could have factored in the lack of an association with that stroke subtype, she said. In general, cerebral infarction is most strongly associated with dietary factors.

The food frequency questionnaire made no distinction between regular and decaffeinated coffee but decaffeinated coffee consumption in the Swedish population is low, Larsson said.

Potential ways that coffee drinking might reduce the risk of stroke include weakening subclinical inflammation, reducing oxidative stress and improving insulin sensitivity, she said.

The study's limitations include the use of a self-administered questionnaire to determine medical history and history of coffee consumption - which inevitably includes some measurement error and misclassification of exposure - and the possibility of an unrecognized confounding factor associated with either low or moderate coffee consumption, Larsson said.

"Some women have avoided consuming coffee because they have thought it is unhealthy. In fact, increasing evidence indicates that moderate coffee consumption may decrease the risk of some diseases such as diabetes,

liver cancer and possibly stroke." More studies on coffee consumption and stroke are needed before firm conclusions can be reached, Larsson said.

Co-authors are Jarmo Virtamo, M.D., and Alicja Wolk, D.MSc. Author disclosures are on the manuscript. The Swedish Council for Working Life and Social Research and the Swedish Research Council for Infrastructure funded the study

http://www.physorg.com/news/2011-03-japan-sixth-infant-death-vaccination.html

Japan reports sixth infant death after vaccination

Japan's health ministry on Thursday reported the death of a sixth infant who recently received vaccinations made by Pfizer or Sanofi-Aventis that have been suspended since last week.

The ministry said the unidentified boy, aged between six months and one year, died seven days after receiving Sanofi Pasteur's ActHIB in combination with a DPT shot for diphtheria, whooping cough and tetanus on February 15. The latest case followed the ministry's earlier reports that five infants under three years old had died since early February after receiving the vaccinations alone or in combination with other drugs.

At least three of the six infants suffered from known pre-existing heart conditions and other illnesses.

The ministry has suspended Prevenar, made by New York-based Pfizer, and ActHIB, made by the Sanofi Pasteur wing of Paris-headquartered Sanofi-Aventis, while it investigates whether they are linked to the children's deaths.

A group of medical experts have said they were not able to identify a specific link between the deaths and the vaccines and the ministry is conducting detailed investigations.

Both shots have been given widely to children around the world for years to prevent bacterial infections causing pneumonia and meningitis, which can be fatal in rare instances.

http://www.scientificamerican.com/article.cfm?id=do-gut-bacteria-worsen-malnutrition

Do Gut Bacteria Worsen Malnutrition?

Human microbiota could be behind why deficient diets leave only some children seriously ill.

By Nicola Jones

A study transplanting gut bacteria from human twins into mice could help to explain why some malnourished children develop kwashiorkor -- a condition that triggers swelling in the belly, fatigue and vulnerability to disease. Researchers hope the work will point the way to better emergency rations for sick children.

The study, presented yesterday by Michelle Smith, a postdoc at Washington University in Saint Louis, Missouri, at the International Human Microbiome congress in Vancouver, Canada, looked at kwashiorkor in children in Malawi. The condition affects tens of thousands of children in Malawi alone and is fatal in up to 15% of cases.

Although poor diet is clearly a factor, no one knows why some children are afflicted and others, living under the same conditions, are not. In tracking 317 pairs of twins in Malawi for the first three years of their lives, the group found that kwashiorkor affected both twins in a pair in only 7% of cases, and in 50% of of cases, only one of the twins. "It's so odd, because they're living together," says Smith.

One possible explanation for why only some malnourished children fall prey to kwashiorkor is that differences in gut bacteria might affect how susceptible people are. Gut bacteria can change how people absorb iron, zinc and vitamins from their food, and have been linked to obesity (see 'Fat people harbour 'fat' microbes').

To investigate, Smith's team, working in Jeff Gordon's microbe genomics lab at Washington University, took faecal samples from some of the Malawian twins and used them to create a set of gut bacteria for mice raised in a completely clean, germ-free environment. Through this they made a near-perfect mimic of the children's gut bacteria, allowing the researchers to see how those bacteria react to changes in diet, and to do other experiments, such as faecal transplants, that would be difficult or impossible with the children themselves. "People think their faeces is just waste -- but it's really useful stuff," says Smith.

In preliminary results presented at the conference, Smith showed how mice with gut bacteria from one set of twins reacted to a series of timed diet regimes. First the mice had three weeks on a typical Malawian diet, consisting of 90% maize (corn) flour and water, and 10% vegetables; then two weeks on a diet of 'ready-to-use therapeutic food', a high-calorie peanut-butter-based food often given to malnourished children in developing countries; and finally two weeks back on the Malawian diet.

The mice with gut bacteria from the sibling with kwashiorkor were found to lose more weight on the maize-and-vegetable diet typical for Malawi, and gain more on the peanut-butter diet, than the mice with gut bacteria from the 'healthy' sibling.

Riding dietary wobbles

One possible conclusion is that the gut bacteria of the sick twin make it hard for the child to absorb the already limited nutrients and calories available in a meagre diet. The 'sick' bacteria were also much more susceptible to

change -- some species flourished, while others died down, altering the overall composition of the population. The 'healthy' gut bacteria, on the other hand, were relatively stable throughout the dietary wobble.

This doesn't prove that gut bacteria composition is the key to why some children get sick and others don't. "I don't think it's not involved. But I can't say it is, yet," says Smith. James Kinross, a clinical researcher at Imperial College London, who was also at the meeting, wonders whether parasitic infections might also be a contributing cause.

But the results point the way to further studies that could help pin down the role of gut bacteria in kwashiorkor, and how they might be harnessed to help sick children. One idea is to transplant 'healthy' gut bacteria into the mice with 'sick' bacteria, and see if this makes a difference. "Their work is very important for developing countries," says Martin Blaser, a microbiologist at New York University, who was also present at Smith's talk. Their method, he adds, could be used to determine the microbiota that help people extract the maximum possible value from food.

Ultimately, Smith would like to identify a bacterium or set of bacteria that protects children from kwashiorkor, and add it to the emergency rations handed out to starving children, or give it to them beforehand. "Maybe we can do earlier interventions -- before they suffer," she says.

http://www.physorg.com/news/2011-03-scientists-neurodegeneration.html

Scientists describe new model for neurodegeneration

UCSF report describes new model for neurodegeneration

A team of scientists at the University of California, San Francisco (UCSF) has developed a new model for how inherited genes contribute to a common but untreatable and incurable neurodegenerative disease. The disease, frontotemporal lobar degeneration, is the second most common cause of dementia before age 65, after Alzheimer's disease.

Based on experiments in worms and mice, the UCSF team's work explains in part why the brain deteriorates in frontotemporal lobar degeneration, which may have implications for the understanding of several neurodegenerative disorders, including Alzheimer's and Parkinson's, as well as different forms of cancer.

"If our findings hold up," said Aimee Kao, an assistant adjunct professor in the Department of Neurology at UCSF, "they may suggest a new way to think about how to treat neurodegenerative diseases." Kao is first author on the study, led by Cynthia Kenyon, PhD, a professor of biochemistry and biophysics at UCSF and director of UCSF's Larry L. Hillblom Center for the Biology of Aging.

Disease Caused By Loss of Neurons

Generally scientists have blamed the mental decline associated with neurodegenerative diseases on the loss of neurons associated with the accumulation of insoluble protein in the brain – sticky plaques that interfere with and ultimately kill the brain's neurons. In frontotemporal lobar degeneration, this loss of neurons happens in the frontal lobe – the part of the brain involved in such higher mental functions as art appreciation and emotional empathy. People with this disease can suffer from progressive difficulties with language, undergo personality and behavioral changes, and usually die within a decade of diagnosis.

The new work suggests that the accumulation of insoluble protein may not be the only cause of cognitive decline in frontotemporal lobar degeneration. Another mechanism could involve how the body deals with injured neurons in the brain.

A significant percentage of patients with frontotemporal lobar degeneration have mutations in the gene that produces a protein called progranulin. Scientists have known that people with these genetic mutations produce too little progranulin protein, but up to now it was unclear what role this played in disease development. Now the work of the UCSF team suggests that progranulin regulates the speed with which dying cells are cleared.

The Speed of Brain Cell Death

Cells in the brain – as in the rest of the human body – die through a process known as apoptosis, or programmed cell death. In a sense, apoptosis is the cellular equivalent of a controlled implosion.

Rather than explode a condemned building in a crowded city and scatter its dust and rubble across surrounding neighborhoods, implosions minimize the fallout. Likewise, apoptosis of neurons prevents them from exploding and damaging the surrounding brain tissue, instead withering them away in protective fashion.

In their paper, Kao, Kenyon and their colleagues show that progranulin normally slows the process of apoptosis. In its absence, however, apoptotic cells are cleared more quickly, probably by neighboring cells, which engulf them.

Using a sophisticated microscope, the UCSF team showed that mutations to the progranulin gene caused cells in the microscopic roundworm C.elegans that were undergoing this programmed cell death to be cleared in about half the time, as compared to normal worms. They also found something similar in engulfing cells called macrophages that were taken from mice. When these cells lacked progranulin, they engulfed other, dying cells

even faster. "In both worms and cultured macrophages," Kao said, "the absence of progranulin cause more rapid clearance of dying cells."

Based on these findings, the team hypothesized that lack of progranulin may affect the ability of cells to recover from an injury. When individual cells are injured, the damage may or may not be fatal. Given enough time, the damaged cell could recover. However, if local engulfing cells are over-eager to remove the damaged cell, the cell may have too little time to recover. If this scenario occurred in the brain, then over time, the cumulative cell loss could lead to neurodegenerative disease.

These findings also have implications in the treatment of cancer, since some aggressive forms of breast, brain and bladder cancer produce increased levels of progranulin. "These cancers may be using progranulin as a sort of 'invisibility shield' to hide from the surveillance of the immune system," Kao said. "Thus, progranulin could represent a druggable target in both neurodegeneration and some forms of cancer."

The study was published online last week by the journal Proceedings of the National Academy of Sciences. Provided by University of California, San Francisco

http://news.discovery.com/earth/what-can-earths-core-tell-us-about-climate-110310.html

Earth's Core ID's Natural and Human-Induced Warming

By Christina Reed | Thu Mar 10, 2011 06:22 PM ET

It could be the beginning of a joke: two bicyclists walk into a bar and ask the bartender what's the correlation between Earth's core, Earth's rotation, and global surface air temperature?

The bartender, a geophysicist during the day, takes out an issue of the Journal of Climate and says, 'I have just what you need.'

Physicists Jean Dickey and Steven Marcus of NASA's Jet Propulsion Laboratory in Pasadena, Calif., working with French colleague geophysicist Olivier de Viron of the Institute of Planetary Physics in Paris, France, took the three variables and spliced out the natural components of surface temperature change that correspond to movements in Earth's core and changes in rotation. They found, as announced in a NASA online features story yesterday, that what remained was a distinct trend of surface temperature warming beginning in 1930 that deviates from the natural oscillations.

Earth's 24-hour rotation around its axis is similar to a biker maintaining a 24 mile-per-hour pace. Slight variations in speed are hallmarks of larger processes taking place. An Iron Man competitor desperately trying to maintain a bike speed of 24 miles per hour still travels faster downhill and slower up hills.

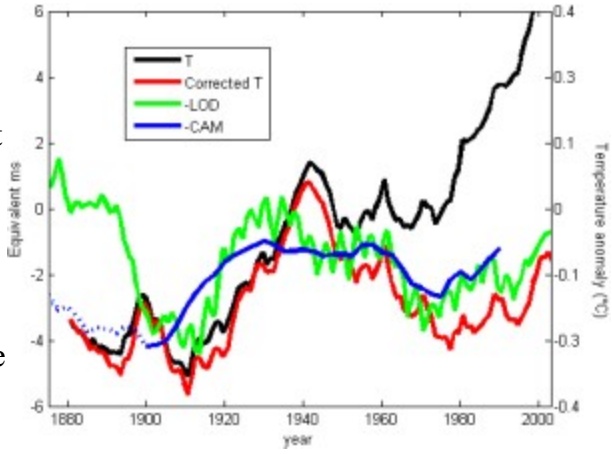
Each year Earth's rotation takes a millisecond longer to spin during the Northern hemisphere's winter but then quickens by a millisecond in the summer. The difference, as explained in the NASA article, is associated with the seasonal interactions that occur between Earth's atmosphere, ocean and land. In this way, the winter months are akin to hills in the rotational terrain.

But on a longer timescale, Earth's rotation can change by as much as 4 milliseconds as it did at the beginning of the 20th century. During these longer timescale variations in rotation the Earth's global average surface air temperature also changes by up to 0.2 degrees Celsius (0.4 degree Fahrenheit) – though no one really knows why.

Dickey and her team wanted to know how much of the warming occurring now could be affiliated with these natural oscillations or if they could see any signal that the warming was human-induced.

In 2009 Dickey and de Viron helped confirm that deep wave oscillations of liquid iron were taking place in the Earth's liquid outer core, by matching the oscillations to changes in the magnetic field at the surface. These deep waves of motion occurred in periods of 85, 50, 35 and 28 years and are at the root of the long-term rotational variations as well.

In the recent study the team compared the liquid iron outer core oscillations with Earth's yearly-averaged rotational speed and two annual global averaged surface air temperature observations dating back to 1880 and 1860. The team found that the trends correlated closely until 1930 – at that time, the surface air temperatures continued to increase, but without corresponding to changes in Earth's length of day or to movements of Earth's core.



Time series of Earth's surface air temperature (black line) and time series corrected for the influence of human activities (red line), Earth's rotation (Length Of Day - green line) and Earth's core angular momentum (blue line).
Credit: NASA/JPL-Université Paris Diderot - Institut de Physique du Globe de Paris.

But if they corrected for human-induced warming, as estimated by computer climate models of Earth's atmosphere and ocean, the trend returned.

"Our research demonstrates that, for the past 160 years, decadal and longer-period changes in atmospheric temperature correspond to changes in Earth's length of day if we remove the very significant effect of atmospheric warming attributed to the buildup of greenhouse gases due to mankind's enterprise," Dickey reported on the NASA website. "Our study implies that human influences on climate during the past 80 years mask the natural balance that exists among Earth's rotation, the core angular momentum and the temperature at Earth's surface."

http://www.eurekalert.org/pub_releases/2011-03/nyph-sbt030811.php

Simple blood test detects early emphysema in smokers before symptoms appear

Researchers say the test, which measures destruction of lung air sacs, could help prevent progression of the common, and fatal, lung disease

NEW YORK - During a regular annual physical exam, blood is usually drawn to check the health of a person's heart, kidneys and liver. Now, researchers at NewYork-Presbyterian Hospital/Weill Cornell Medical Center say a blood test that detects the early development of emphysema -- well before symptoms occur -- may someday also be offered.

In the March 11 online edition of the American Journal of Respiratory and Critical Care Medicine, the researchers say that because most cases of emphysema are caused by smoking, the test they are developing can warn smokers about impending development of the untreatable disease -- which is currently a major cause of disability and death in the U.S.

Not all smokers develop emphysema, but those who find out they are at risk will be motivated to quit to halt progression of the disease, says the study's lead investigator, Dr. Ronald G. Crystal, chairman and professor of genetic medicine and the Bruce Webster Professor of Internal Medicine at Weill Cornell Medical College and chief of the Division of Pulmonary and Critical Care Medicine at NewYork-Presbyterian Hospital/Weill Cornell Medical Center.

"We know, from other studies, that smokers who learn from objective evidence that their health is in danger are much more likely to quit," he says. "That is the only thing that will help them avoid this deadly disorder."

Emphysema and chronic bronchitis are the twin disorders that make up chronic obstructive pulmonary disease (COPD), which is now the fourth leading cause of death in Americans. Given the aging population, COPD is soon expected to move up to third in mortality prevalence, Dr. Crystal says.

The new test measures particles that are shed by tiny blood vessels known as capillaries that surround air sacs (alveoli) in lungs. These particles are debris shed by ongoing injury to the air sacs -- damage that eventually results in devastation of the sacs and the "Swiss cheese" appearance of the lungs. The alveoli are where critical gas exchanges occur: blood in the capillaries brings carbon dioxide from the rest of the body for release into the air sacs, and the oxygen in the sacs (taken in from breathing) is taken up by the blood and transported to the rest of the body.

As the sacs are destroyed, people develop shortness of breath because they cannot take in enough oxygen to feed the body and eventually cannot remove carbon dioxide from the blood.

Dr. Crystal and his colleagues reasoned that as capillaries surrounding the air sacs are being injured, the debris would be carried out by the blood supply and could potentially be quantified as a disease biomarker. So they began to look for evidence of what they called endothelial microparticles (EMP).

"Our blood vessels are always being replenished, so we all have some level of EMPs in our blood," he says. "What we are looking for are elevated levels of EMPs. For smokers, this is the equivalent of a smoke detector sounding its alarm; elevated levels of EMPs suggest their air sacs are being injured and it is time to act."

To do this, the researchers enrolled three groups of people -- healthy nonsmokers, healthy smokers, and smokers with early evidence of lung destruction. Study participants had their medical histories taken, and to gauge lung function in these participants, all underwent two pulmonary function tests. One is spirometry, which measures the volume and speed of air as it is inhaled and exhaled from the lungs. The other, known as DLCO, is the only lung function test available today that can detect emphysema in patients. It uses a machine that measures the ability of gases to diffuse across the alveolar-capillary membrane.

The researchers found a 95 percent positive correlation between elevated EMPs in the blood and an abnormal DLCO test result, meaning that it detected nearly all verified cases of early emphysema in participants.

Two other independent groups of participants were then given the same group of tests -- spirometry, DLCO and the EMP blood test -- and, once again, a positive EMP finding correlated with an abnormal DLCO 95 percent of the time. Differences in the spirometry findings had no bearing on results of DLCO or EMP.

DLCO, which must be administered by a pulmonologist, is most often used to confirm a suspicion of emphysema, Dr. Crystal says. By contrast, the EMP blood test is designed to be a simple, low-cost screening tool that can pick up development of emphysema in individuals who show no signs of the disorder.

"We need a blood test that can be administered to the 20 percent of American adults who smoke as well as nonsmokers exposed to secondhand smoke -- all who may not understand their risk of developing this progressive lung disease," says Dr. Crystal.

The researchers are conducting further studies of the EMP test in larger groups of participants in order to validate these initial findings.

The study was funded by grants from the National Institutes of Health.

Co-authors include Drs. Cynthia Gordon, Kirana Gudi, Anja Krause, Rachel Sackrowitz, Ben-Gary Harvey andYael Strulovici-Barel, all from NewYork-Presbyterian/Weill Cornell and Dr. Jason Mezey from Cornell University, Ithaca, N.Y.

http://www.eurekalert.org/pub_releases/2011-03/uoth-fsp031111.php

Finding shows potential way to protect neurons in Parkinson's, Alzheimer's, ALS

SAN ANTONIO — *Cell biologists pondering the death of neurons — brain cells — said today that by eliminating one ingredient from the cellular machinery, they prolonged the life of neurons stressed by a pesticide chemical.*

The finding identifies a potential therapeutic target to slow changes that lead to neurodegenerative disorders such as Parkinson's and Alzheimer's diseases. The researchers, from The University of Texas Health Science Center San Antonio, found that neurons lacking a substance called caspase-2 were better able to withstand pesticide-induced damage to energy centers known as mitochondria.

Master switch

Caspase-2 appears to be a master switch that can trigger either cell death or survival depending on the amount of cellular damage, the team found. Neurons that lacked caspase-2 showed an increase in protective activities, including the efficient breakdown of obsolete or used proteins. This process, called autophagy, delays cell death. "This research shows, for the first time, that in the absence of caspase-2 neurons increase autophagy to survive," said study co-author Marisa Lopez-Cruzan, Ph.D., investigator in the cellular and structural biology department at the Health Science Center.

Role of energy centers

Evidence suggests that mitochondrial dysfunction plays an important role in neuronal death in conditions such as Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease) and Huntington's disease.

"Identifying initiators in the cell death process is important for determining therapeutic approaches to provide the maximum protection of neurons during neurodegenerative conditions," said senior author Brian Herman, Ph.D., vice president for research and professor of cellular and structural biology at the Health Science Center.

Young adult mice

The team studied neurons from young adult mice. This was intended to model the early changes that take place in neurodegenerative diseases. The research is in the March 11 issue of the Journal of Biological Chemistry.

Dr. Lopez-Cruzan, director of Dr. Herman's laboratory, came up with the idea that caspase-2 protects cells from mitochondrial stress. Meenakshi Tiwari, Ph.D., postdoctoral fellow, expanded upon the initial work and is first author of the paper.

The work was supported by the National Institute on Aging and is part of a second National Institutes of Health MERIT award to Dr. Herman.

http://www.eurekalert.org/pub_releases/2011-03/iotm-eid031111.php

Extra iron doesn't help many pregnant women

Although universal prenatal supplementation with iron is recommended, an extra intake of iron does not noticeably benefit pregnant women, except when they are anemic.

This was observed by researchers of the Institute of Tropical Medicine Antwerp and colleagues who followed more than a thousand pregnant women in Burkina Faso.

Our body needs iron to produce hemoglobin, the substance in our red blood cells responsible for the transport of oxygen through our body. In Western countries anemia – a shortage of oxygen transporters – is rare, but in Africa up to half of all women are anemic. Of the 1268 pregnant women in this study, 43% was anemic.

Half of those women received daily pills with 60 milligrams of iron (plus folic acid); the other half received 30 mg of iron (plus folic acid, zinc, vitamins A and C and other micronutrients). Chance decided who got what. The women took the pills until 3 months after delivery. At the end of the study, all women ended up with about the same levels of iron in their blood, regardless of how much iron they had taken. They al had around 11 grams of hemoglobin per deciliter of blood, say slightly below normal.

During pregnancy, when also the growing child needs oxygen, women need more iron than normally, certainly towards the end of their pregnancy. But the administration of extra iron to the 'normal' women could not prevent their hemoglobin levels from (slightly) dropping. "The benefit of iron supplements in nonanemic women is unclear", the authors conclude in The American Journal of Clinical Nutrition.

In Africa, where many people are malnourished, and where parasites also take their part, many women suffer from iron-poor blood. That of course has to be supplemented. In anemic women the pills made the iron levels go up, to the same level as in the other pregnant women: a bit below normal.

http://www.newscientist.com/article/mg20928033.700-tumours-could-be-the-ancestors-of-animals.html

Tumours could be the ancestors of animals

*** 11 March 2011 by Colin Barras**

CANCER remains a formidable foe even 40 years after Richard Nixon officially declared war on it.

A new and controversial hypothesis now offers hope that the war can ultimately be won. It suggests tumours have a limited ability to evade modern therapies - a consequence of the idea that cancer is our most distant animal ancestor, a "living fossil" from over 600 million years ago.

Some cancers evolve resistance to a treatment within a few years. One possible explanation for this is that the cells within a tumour act independently, competing with one another via natural selection to evolve therapy-dodging innovations.

Astrobiologists Charles Lineweaver at the Australian National University in Canberra and Paul Davies at Arizona State University in Tempe have an alternative explanation. They say that evidence of basic cellular cooperation within tumours suggests cancers are a throwback from the origin of the animal kingdom - and that any ability to resist modern drugs relies on an ancient and ultimately limited array of survival tactics.

Their hypothesis builds on an old idea that suggests a link between cancer and the origin of multicellular animals, sometime before 600 million years ago. For billions of years before that point, the animals' single-celled ancestors replicated with reckless abandon. Once organisms contained multiple cells, however, replication had to become more restrained, to avoid adverse effects on the organism.

Cancer is thought to be triggered by a malfunction of the genes that try to hold back this uncontrolled replication. But Lineweaver and Davies go further: cancer is not simply linked to the evolution of animals - it was the earliest animals. They believe these organisms had cracked the problem of runaway replication but they still lacked total control over cell growth and proliferation.

The hypothesis helps to explain some of the more unusual features of tumours, says Lineweaver. Some cancer cells build a network of blood vessels, a process known as angiogenesis, to bring nutrients into the tumour - evidence of tumour-wide cooperation. Other cells gain the ability to spread to other tissues, or metastasise, which is difficult to explain if all cancer cells act independently.

Lineweaver and Davies think the genetic toolkit at work in these first animals is buried within all of us. The genes that came later might have tinkered with it, but whenever those later additions malfunction the ancient genes can revert to their initial function.

Consequently, a tumour is not a collection of independently evolving cells, like bacteria, with almost infinite potential to evolve resistance to therapy. It is a group of largely cooperating cells relying on a finite collection of survival strategies that were locked in place over half a billion years ago (Physical Biology, DOI: 10.1088/1478-3975/8/1/015001). Reactions to Lineweaver and Davies's idea vary from cautious enthusiasm to outright scepticism. Carlo Maley at the University of California in San Francisco, who studies the evolutionary processes at work in cancer, is receptive: "They make a bunch of interesting predictions," he says.

Others are more guarded. It is an "imaginative metaphor", says Mansi Srivastava at the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, who studies the evolution of genes including those involved with cancer. However, she thinks the idea of cancer as a living fossil from the dawn of animal life is a step too far. "There is no evidence to believe that the ability to develop blood vessels is an ancient feature of animals."

Lineweaver disagrees: "Fully developed angiogenesis had to have evolved from proto-angiogenesis," he says. "I think it's clear that some form of proto-angiogenesis was very important for the earliest animals."

Genetic profiling may soon help to test the hypothesis, says Lineweaver. The ways a particular cancer responds to treatment in different people should correlate with each other, he says, because they should share strategies for dealing with toxins that were developed in the earliest animals.

Even if cancer does have a limited ability to resist treatment, though, Maley has a reality check. If the war on cancer has taught us anything, it is that battling even a predictable cancer will remain "plenty hard" in the short term.

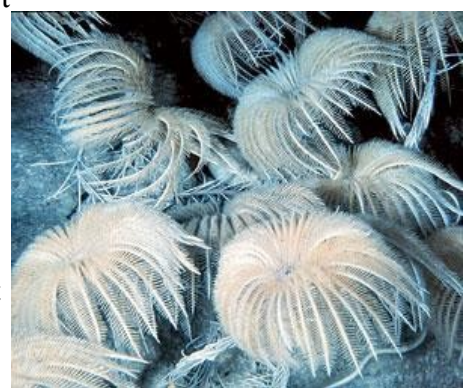
http://www.newscientist.com/article/mg20928033.900-lost-world-hints-at-life-in-the-mesozoic.html

Lost world hints at life in the Mesozoic

*** 11 March 2011 by Wendy Zukerman**

IN AN echo of Arthur Conan Doyle's famous book, a lost world containing a community of animals that has changed little since Tyrannosaurus and Triceratops walked the Earth has been found.

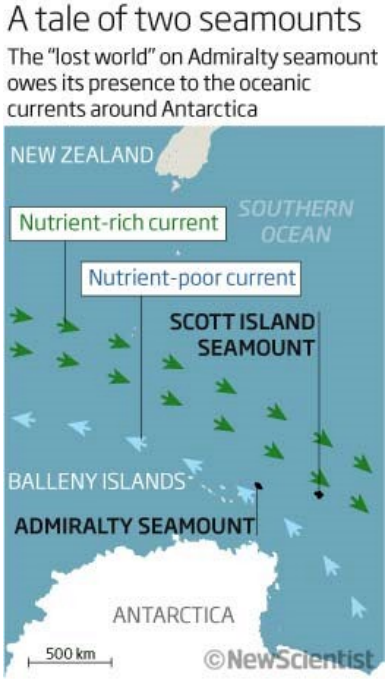
But while Conan Doyle's lost world was on a South American plateau, its real life equivalent lies on a submerged mountain off the Antarctic coast. Rather than dinosaurs, this lost world is filled with crinoids, the stalked cousins of sea stars and sea urchins. Also known as sea lilies, crinoids were abundant in the shallow seas of the Mesozoic, 250 to 65 million years ago. Today, however, they were only thought to exist in small numbers in the deep sea, possibly because of pressure from recently evolved predators.



They don't make 'em like they used to (Image: Charles Messing)

David Bowden at the National Institute of Water and Atmospheric Research in Auckland, New Zealand, and colleagues discovered over 1000 crinoids belonging to an as yet undescribed species on Admiralty seamount (see map) during an International Polar Year Census of Antarctic Marine Life voyage. "We were surprised to find such extensive populations," he says.

The biologists also surveyed the neighbouring Scott Island seamount, but intriguingly they spotted only 22 crinoids there (Deep-Sea Research Part II, DOI: 10.1016/j.dsr2.2010.09.006).



The crinoids might have survived on Admiralty seamount because it is bathed in nutrient-poor waters from the Antarctic coast, which generally produce too little food to sustain predators, Bowden says. In contrast, Scott Island is influenced by nutrient-rich waters from the north, and predators are more common.

The accumulation of crinoid skeletons at Admiralty seamount suggests this community may have been thriving for around 25,000 years, says Bowden. Skeletal samples taken from the site could not be accurately carbon dated, so the team now plans to date rock samples to establish its age.

Although the community appears to be relatively young, the creatures seem so similar to their Mesozoic ancestors that the way they feed and position themselves to form a community is probably unchanged, says Tim O'Hara at the Melbourne Museum, Australia. "This way of life has been extinguished from most of the sea," he says. "Now we can see it in all of its glory."

"It's extraordinary that they survived," says Charles Messing at Nova Southeastern University Oceanographic Center in Florida, who was not involved in the study. "It's just wonderful. When I first saw those pictures I thought: when do we go back?"

http://www.newscientist.com/article/mg20928033.200-half-of-germanys-doctors-prescribe-placebos.html

Half of Germany's doctors prescribe placebos

PRESCRIPTIONS of placebos are booming in Germany and Switzerland, reveals a report released last week by the German Medical Association (GMA).

For example, 53 per cent of the doctors from the Medical University of Hannover said they would prescribe placebos such as vitamin pills and homeopathic remedies. Half the doctors in a national Swiss survey agreed.

Their use of such treatments contrasts with the UK, where homeopathic treatments have been rejected by scientists. However, "physicians should be made aware of the value of the placebo effect in the daily treatment of patients", says Christoph Fuchs, chief executive of the GMA. "Their use is of enormous importance for medical practice." The report cautions that placebos should be prescribed only for very minor conditions or where traditional therapies are not available.

http://www.eurekalert.org/pub_releases/2011-03/uoca-cs031111.php

'Good cholesterol' structure identified, could help explain protective effects

CINCINNATI—*University of Cincinnati (UC) researchers have determined the structure of human HDL cholesterol and say the finding could help explain how this "fat packet" protects against cardiovascular diseases, including heart attack and stroke.*

The study, led by W. Sean Davidson, PhD, professor in UC's pathology and laboratory medicine department, appears online ahead of print March 13, 2011, in the journal Nature Structural & Molecular Biology.

HDL (high-density lipoproteins) also known as "good cholesterol," are packets of protein and fat that deliver fat to specific locations within the body. There is an increasing effort to create drugs that help to raise levels of HDL working in conjunction with existing drugs that lower "bad cholesterol," or low-density lipoproteins (LDL).

Studies of synthetically derived HDL have shown that an abundant protein in HDL, apolipoprotein A-I, plays a key role in HDL's cardioprotective anti-inflammatory and anti-oxidative properties.

"Unfortunately, we've known very little about the molecular details that explain HDL's protective effects," says Davidson. "A major reason for this is an almost complete lack of understanding of HDL's structure and how it interacts with other important plasma factors."

Rong Huang, PhD, a post-doctoral fellow in Davidson's laboratory, has isolated human HDL and analyzed its 3-D structure as it circulates in human plasma.

"Previous studies have only focused on synthetic HDL made in the test tube," Davidson says. "By isolating human HDL, we were able to focus on the broad range of HDL particles actually circulating in humans."

Team members used a series of sophisticated spectroscopic and mass spectrometric techniques to study HDL and have found that proteins of HDL form a cage-like structure that encapsulates its fatty cargo. They determined that most of the HDL particles circulating in human plasma are remarkably similar in structure; however, they found evidence that the particles have a twisting or shock absorber-like motion that allows them to adapt to changes in particle fat content.

By determining the structure of HDL, Davidson and his team were able to conclude that the majority of physiological interactions occurring with HDL - including its twisting movements - occur at the particle surface, which is dominated by the cardioprotective protein apolipoprotein A-I.

This monopolization of the particle surface, Davidson says, suggests that other proteins have very little room to bind to HDL and probably have to interact with the protein itself, which could explain how apolipoprotein A-I plays such a dominant role in HDL function and its protective effects. "This work presents the first detailed models of human plasma HDL and has important implications for understanding key interactions in plasma that modulate its protective functions in the context of cardiovascular disease," says Davidson.

The study was funded by grants from the National Institutes of Health and its National Heart, Lung, and Blood Institute, as well as funds from the American Heart Association.

http://www.physorg.com/news/2011-03-method-infer-tumors-evolve.html

With new method, researchers are able to infer how tumors evolve and spread

A new method of analyzing cancerous tumors developed by scientists at Cold Spring Harbor Laboratory (CSHL) suggests that tumors may not evolve gradually, but rather in punctuated or staccato-like bursts.

It is a finding that has already shed new light on the process of tumor growth and metastasis, and may help in the development of new methods to clinically evaluate tumors.

The new analytic method, devised by CSHL Professor Michael Wigler and colleagues, features a process called single cell sequencing (SNS), which enables accurate quantification of genomic copy number within a single cell nucleus. Genomic copy number refers to the amount of DNA in the nucleus. In cancer, portions of the genome are amplified or deleted, giving rise to extra or missing copies of key genes and interfering with mechanisms that normally control cell growth.

In a study published today in the journal Nature, "we demonstrated that we can obtain accurate and high-resolution copy number profiles by sequencing a single cell from a cancerous tumor," says Wigler, "and that by examining multiple cells from the same cancer, we can make inferences about how the cancer evolved and spread." The CSHL team also includes Professor W. Richard McCombie, Assistant Professor Alex Krasnitz and Research Professor James Hicks. Nicholas Navin, the paper's first author, was a graduate student while pursuing the research at CSHL and is now Assistant Professor at MD Anderson Cancer Center in Texas.

The importance of cancer's heterogeneity

It has been very difficult for scientists to translate their growing ability to classify tumors at the molecular level into methods and tests that can be used in the clinic to analyze tumors in actual patients. But basic

research has firmly established that cancer is highly heterogeneous, meaning that cancers of a certain type, for instance cancers of the breast or lung or colon, can be subdivided into many distinct subtypes. Unique markers have been found in a number of cancer subtypes, such as abnormally high levels of the receptor protein encoded by the HER2neu gene, which in a subset of breast cancer cases is a causal factor in oncogenesis. The HER2neu receptor is the target for the pathbreaking drug Herceptin™ (Genentech Roche).

In the CSHL team's just-published study, the two sampled tumors were known in advance – because of prior study -- to represent distinct types. Both were primary invasive breast cancer tumors of the so-called "triple-negative" type, generally regarded as the most aggressive form of breast cancer. One tumor sample was known from prior testing to be polygenomic: composed of distinct populations of tumor cells, whose number, genomic type and evolutionary history were not readily measurable using conventional techniques. The other sampled tumor was monogenomic: composed of cells of a single genetic type. Unlike the first sample, this one had metastasized, to the liver, and samples of that tumor were also subjected to analysis.

Using SNS, in concert with whole-genome amplification and next-generation sequencing, the CHSL team was able to show that in fact three distinct subpopulations of tumor cells were present. "By SNS we could now see that each of these subpopulations was composed of cells that shared highly similar copy number profiles," says Navin. "We could infer that these most probably represent three distinct clonal expansions of the tumor."

Distinct clonal populations as evolutionary 'winners'

Cancer has long been understood to be a clonal disease at the cellular level, with what in evolutionary terms might be called "successful" tumor cells providing the genetic template for the next generation of tumor-cell offspring. The cancer cells comprising the rapidly expanding malignant clone, it is thought, are those best able to survive in the hostile environment of the growing tumor, into which the body's own immune cells have migrated and perhaps also toxic chemotherapy drugs have been introduced. This is one way of understanding why cancers are so tough to combat, and why they are able to survive even the application of cytotoxic therapies. In short, cancer cells are often able to evolve around these.

It has been theorized that genetically heterogeneous tumor cell populations become mixed via gradual evolution. The CSHL team, in contrast, suggests the evolution is likely punctuated. "It's a very complicated matter to try to determine a given tumor's genetic evolution," says Hicks of the CSHL team. "The different groups of cells are geographically and anatomically intertwined. In evolutionary terms, you might think of them as distinct but intermixed 'tribes,' or subspecies. It's important to keep in mind that tumors are chaotic places. There's always a certain amount of chaotic evolution taking place, some of it reflected in rearrangement of chromosomes and some in single base-pair changes in the DNA of individual tumor cells. But our results, although based so far on a limited sample size, suggest that major clonal expansion events are relatively infrequent and may provide accessible targets for targeted treatments"

Implications for understanding metastasis

The second breast cancer sample analyzed by the team was of a single genomic type, but the team was able to determine that the liver metastasis to which it had given rise was very closely related, in genomic terms. "The data suggest the primary tumor mass formed by a single clonal expansion and that one of the cells from this event subsequently seeded the metastatic tumor, with little further evolution," according to Navin. "Although closely related, primary and metastatic tumor cells were cleanly separated, indicating to us that the two populations had not mixed" since the origin of the metastasis. Further, he noted, "differences in the profiles that distinguish primary and metastatic tumor populations were in the degree of copy number changes."

A method called chromosomal breakpoint analysis was the means by which the team drew inferences about the relationships between various tumor cell subpopulations. "The history of the cell is written in these breakpoints," explains Hicks. "They are the product of mutational events, the rearrangements of DNA that have occurred, and they don't go away." Generally speaking, these events are additive, a key concept that enabled the CSHL team to say that the genetic provenance of a cell is written in its DNA. The evolutionary history of the polygenomic tumor sample studied was traced by tracking 657 distinct chromosomal breakpoints. Tumor cells of all three clonal "subspecies" shared about half the mutational events; only a fraction shared another significant number of mutations; and a still smaller fraction shared yet another wave of mutations.

A significant fraction of tumor cells – up to 30% -- contained some combination of DNA deletions and additions that made them appear normal, in terms of their total DNA content. These cells, called "pseudodiploid" by the researchers, appear to be cancerous but are not part of the major clonal expansions. The team's method provides the first means of identifying such cells, which are not distinguishable using conventional methods of tumor characterization. One hypothesis holds that such cells are potential sources of future clonal events; another, that they may be important in the process of metastasis.

"We want to learn how a metastasis grows," said Hicks, "and we now have the ability to do that at a very detailed level. In a typical blood draw taken from a cancer patient, you will typically see between five and 20 circulating tumor cells, a mark of metastasis. We'll be able to look at every one of them and see if, for example, there's a new clone that is different from the cell populations in the primary tumor. By working at a granular level, cell by cell, we can look deeply into a metastasis and see how it got built."

More information: "Tumor Evolution Inferred by Single Cell Sequencing" appears online ahead of print in Nature on March 13, 2011. Provided by Cold Spring Harbor Laboratory

http://www.thedailybeast.com/blogs-and-stories/2011-03-13/why-japans-nuclear-meltdown-is-no-chernobyl/

Why Japan's Nuclear Meltdown is no Chernobyl

Despite the scary race to prevent two meltdowns in Japan, the man who led the Chernobyl response explains how advances in nuclear design and the swift response will prevent any damage along the lines of 1986 Soviet disaster.

The partial meltdown of Reactor 3 at the Fukushima Daiichi power station is the most serious nuclear accident since Chernobyl, but Russian experts say the differences mercifully outweigh the similarities.

Indeed it may be thanks in part to the terrible legacy of the April 1986 disaster that Fukushima's meltdown can be contained. "The accident at Fukushima shows that experts around the world drew some important lessons from what happened at Chernobyl," said nuclear engineer Ilgiz Iskhatov, who was decorated for his role in containing the fallout of the Chernobyl blast. "Now nuclear power-station designs and safety systems are capable of withstanding much more serious accidents [than Chernobyl]."

The meltdown of the Chernobyl reactor blew the unit's casing apart and voided the core to the atmosphere. Fukushima hasn't yet melted through the reactor vessel, thanks to engineers pumping seawater into the cooling systems.

"There is no question of a Chernobyl situation or of anything like the same threat to human health and safety," said Rafael Arutyunyan, deputy head of the Russian Academy of Sciences' Institute of Nuclear Energy Development Security. "An accident like Chernobyl cannot happen again—this is a reactor of a different generation. Even in the worst-case scenario of a total coolant failure, the radiation released will be hundreds of times less than from Chernobyl."

Just as important, said Iskhatov, the Japanese authorities have "acted quickly and effectively to communicate with the local residents - they don't treat their population like idiots like ours did." "Chernobyl taught the world of nuclear reactor designers that they have to be ready for the most unforeseen failures, the most extreme situations," said Iskhatov.

In the immediate aftermath of the Chernobyl blast, Soviet authorities tried to hush up the accident, and the world was alerted to the deadly cloud of nuclear fallout traveling across Northern Europe when radiation alarms went off at the Forsmark nuclear power station in Sweden, more than 1,000 kilometers north of the accident site. Evacuation of the Chernobyl area did not begin until 24 hours after the initial accident, which killed 54 people directly and as many as 4,000 from radiation-related illnesses. In Japan, within hours of the initial alert, Japanese authorities evacuated 200,000 people from the area of Fukushima. Russia has also sent two teams of emergency rescue specialists to Japan and promised extra deliveries of natural gas, though no Russian nuclear experts have been requested or sent.

According to a detailed Soviet report released to the public after the fall of communism, the Chernobyl blast was caused by a sudden, catastrophic spike in temperature at the reactor that caused cooling graphite rods to shatter, which in turn allowed a runaway nuclear reaction that within three seconds produced more than a hundred times the unit's usual heat output. The coolant from burst pipes flashed into steam, blowing a 2,000-ton steel and concrete lid off the reactor core and spreading radiation across the Soviet Union and Europe.

Mercifully, the accident at Fukushima seems to be far less serious. Japanese Prime Minister Naoto Kan said Sunday the nuclear crisis in the northeast of the country was "fundamentally different from the Chernobyl accident" - and he seems to be right, unlike the Soviet authorities in 1986 who did everything to downplay and deny the seriousness of Chernobyl. According to initial reports, two separate reactors at Fukushima were put out of action by the earthquake: Reactor 1, which suffered an explosion in the turbine hall causing a small escape of radiation, and Reactor 3, which appears to have partially melted down after a power failure to both its main and backup cooling systems. On Sunday night, Japanese technicians were still trying to bring the two under control; cooling stations at two of three reactors at the neighboring Daini power station had been restored.

What's happening now is "more akin to the reactor accident at Three Mile Island in Pennsylvania in 1979 than Chernobyl," said Aleksandr Uvarov, editor of the Moscow-based Web portal AtomInfo-Center. At Three Mile Island, a coolant failure led to a partial reactor core meltdown—though like in Fukushima, the casing of the Three Mile Island reactor wasn't breached, unlike the catastrophic explosion that blew apart Chernobyl.

Japanese Chief Cabinet Secretary Yukio Edano confirmed Sunday to reporters that a partial meltdown in Reactor 3 is "highly possible," and the presence of radioactive cesium in leaked radiation suggests that fuel rods have already melted, according to U.S. nuclear physicist Ken Bergeron. "The containment building at this plant is certainly stronger than that at Chernobyl but a lot less strong than at Three Mile Island, so time will tell," he said.

Fukushima is avoiding total meltdown so far—but pumping in seawater is "an act of desperation," said Robert Alvarez of Washington's Institute for Policy Studies. "I would describe this measure as a ‘Hail Mary' pass"—a last-ditch attempt to save a desperate situation. Still, had it not been for the lessons learned from Chernobyl, the disaster could have been far worse. "Chernobyl taught the world of nuclear-reactor designers that they have to be ready for the most unforeseen failures, the most extreme situations," said Iskhatov.